```
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
FILE 'USPAT' ENTERED AT 17:02:40 ON 15 JUL 1999

  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *         U. S.   P A T E N T   T E X T   F I L E               *
  *                                                               *
  *  THE WEEKLY PATENT TEXT AND IMAGE DATA IS CURRENT             *
  *  THROUGH July 13,1999                                         *
  *                                                               *
  *                                                               *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> s (raloxifen or droloxifen or centchroman)

             9 RALOXIFEN
             1 DROLOXIFEN
            25 CENTCHROMAN
L1          34 (RALOXIFEN OR DROLOXIFEN OR CENTCHROMAN)

=> s (lhrh oe lutein?(w)hormone#(w)releas?(w)hormone#)

           712 LHRH
          9622 OE
          1928 LUTEIN?
             0 LHRH OE LUTEIN?
                 (LHRH(W)OE(W)LUTEIN?)
         23706 HORMONE#
<------User Break------>
u
SEARCH ENDED BY USER

=> s (lhrh or lutein?(w)hormone#(w)releas?(w)hormone#)

           712 LHRH
          1928 LUTEIN?
         23706 HORMONE#
        607798 RELEAS?
         23706 HORMONE#
           579 LUTEIN?(W)HORMONE#(W)RELEAS?(W)HORMONE#
L2         977 (LHRH OR LUTEIN?(W)HORMONE#(W)RELEAS?(W)HORMONE#)

=> s l1 and l2

L3           0 L1 AND L2
```

* * * * * * RECONNECTED TO U.S. Patent & Trademark Office * * * * * *
SESSION RESUMED IN FILE 'USPAT' AT 17:22:08 ON 15 JUL 1999
FILE 'USPAT' ENTERED AT 17:22:08 ON 15 JUL 1999

=> d his

(FILE 'USPAT' ENTERED AT 17:02:40 ON 15 JUL 1999)
L1 34 S (RALOXIFEN OR DROLOXIFEN OR CENTCHROMAN)
L2 977 S (LHRH OR LUTEIN?(W)HORMONE#(W)RELEAS?(W)HORMONE#)
L3 0 S L1 AND L2

=> s (RALOXIFENe OR DROLOXIFENe OR CENTCHROMAN)

167 RALOXIFENE
29 DROLOXIFENE
25 CENTCHROMAN
L4 205 (RALOXIFENE OR DROLOXIFENE OR CENTCHROMAN)

=> s l2 and l4

L5 10 L2 AND L4

=> s l2(p)l4

L6 1 L2(P)L4

=> d l6 1

1. 5,770,603, Jun. 23, 1998, Quinazoline derivatives; Keith Hopkinson Gibson, 514/259; 544/293 [IMAGE AVAILABLE]

=> d l6 kwic 1

US PAT NO: 5,770,603 [IMAGE AVAILABLE] L6: 1 of 1

SUMMARY:

BSUM(85)

The . . . for example etoposide and camptothecin; biological response modifiers, for example interferon; anti-hormones, for example antioestrogens such as tamoxifen, toremifene or **raloxifene**, for example antiandrogens such as 4'-cyano-3-(4-fluorophenylsulphonyl)-2-hydroxy-2-methyl-3'-(trifluoromethyl)-propionanilide (bicalutamide), flutamide, nilutamide or cyproterone acetate, or, for example **LHRH** antagonists or **LHRH** agonists such as goserelin, leuprorelin or buserelin and hormone synthesis inhibitors, for example aromatase inhibitors such as those disclosed in. . .

=> d l5 1-10

1. 5,919,815, Jul. 6, 1999, Taxane compounds and compositions; Matthews O. Bradley, et al., 514/449; 549/510 [IMAGE AVAILABLE]

2. 5,843,962, Dec. 1, 1998, Methods of inhibiting ovarian dysgenesis, delayed puberty, or sexual infantilism; Jeffrey A. Dodge, 514/324, 422

[IMAGE AVAILABLE]

3. 5,795,909, Aug. 18, 1998, DHA-pharmaceutical agent conjugates of taxanes; Victor E. Shashoua, et al., 514/449, 549 [IMAGE AVAILABLE]

4. 5,770,603, Jun. 23, 1998, Quinazoline derivatives; Keith Hopkinson Gibson, 514/259; 544/293 [IMAGE AVAILABLE]

5. 5,760,060, Jun. 2, 1998, Methods of inhibiting ovarian dysgenesis, delayed puberty, or sexual infantilism; Jeffrey A. Dodge, 514/324, 422, 443 [IMAGE AVAILABLE]

6. 5,719,165, Feb. 17, 1998, Methods of inhibiting ovarian dysgenesis, delayed puberty, or sexual infantilism; Jeffrey A. Dodge, 514/324, 422, 443 [IMAGE AVAILABLE]

7. 5,552,417, Sep. 3, 1996, Methods of Inhibiting sexual precocity; Jeffrey A. Dodge, 514/324, 422, 443 [IMAGE AVAILABLE]

8. 5,462,949, Oct. 31, 1995, Methods of inhibiting fertility in women; Charles D. Jones, et al., 514/324 [IMAGE AVAILABLE]

9. 5,451,590, Sep. 19, 1995, Methods of inhibiting sexual precocity; Jeffrey A. Dodge, 514/324 [IMAGE AVAILABLE]

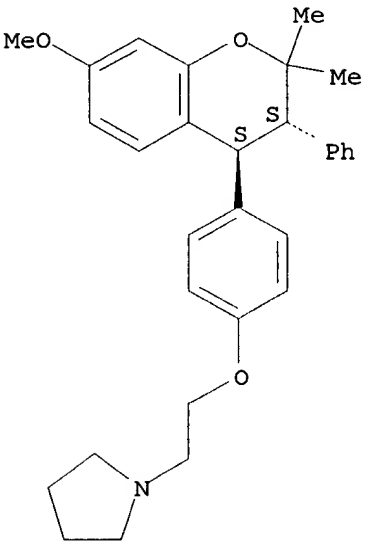
10. 5,451,589, Sep. 19, 1995, Methods of inhibiting ovarian dysgenesis, delayed puberty, or sexual infantilism; Jeffrey A. Dodge, 514/324, 422, 443 [IMAGE AVAILABLE]

=> d 15 kwic 1-10

```
=> e raloxifen/cn

E1            1      RALOX BHT/CN
E2            1      RALOX LC/CN
E3            0 --> RALOXIFEN/CN
E4            1      RALOXIFENE/CN
E5            1      RALOXIFENE HYDROCHLORIDE/CN
E6            3      RALSTONITE/CN
E7            1      RALSTONITE (ALF2(OH))/CN
E8            1      RALSTONITE (ALF2(OH).1/2H2O)/CN
E9            1      RALTITREXED/CN
E10           1      RALUBEN/CN
E11           1      RALUFON DCH/CN
E12           1      RALUFON DL/CN

=> e droloxifen/cn

E1            1      DROLBAN/CN
E2            1      DROLEPTAN/CN
E3            0 --> DROLOXIFEN/CN
E4            1      DROLOXIFENE/CN
E5            1      DROLOXIFENE CITRATE/CN
E6            1      DROLOXIFENE N-OXIDE/CN
E7            1      DROLUENE 10/CN
E8            1      DROLUENE 2.5/CN
E9            1      DROLUENE 25/CN
E10           1      DROLUENE 5/CN
E11           1      DROME PROTEIN (ILE-149) (HUMAN CLONE PBL-2)/CN
E12           1      DROME PROTEIN (MET-149) (HUMAN CLONE PBL-2)/CN

=> e centchroman/cn

E1            1      CENTBUTINDOLE/CN
E2            1      CENTBUTINDOLE, (-)-/CN
E3            1 --> CENTCHROMAN/CN
E4            1      CENTCHROMAN HYDROCHLORIDE/CN
E5            1      CENTDAROL/CN
E6            1      CENTDARONE/CN
E7            1      CENTEDRIN/CN
E8            1      CENTEDRINE/CN
E9            1      CENTELLA ASIATICA, EXT./CN
E10           1      CENTELLA EXT./CN
E11           1      CENTELLASE/CN
E12           1      CENTHAQUIN/CN

=> s e3

L1            1 CENTCHROMAN/CN

=> d l1 1


L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 1999 ACS
RN   31477-60-8  REGISTRY
CN   Pyrrolidine,
1-[2-[4-[(3R,4R)-3,4-dihydro-7-methoxy-2,2-dimethyl-3-phenyl-
     2H-1-benzopyran-4-yl]phenoxy]ethyl]-, rel- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Pyrrolidine, 1-[2-[4-(3,4-dihydro-7-methoxy-2,2-dimethyl-3-phenyl-2H-1-
```

benzopyran-4-yl)phenoxy]ethyl]-, trans-
CN Pyrrolidine, 1-[2-[p-(7-methoxy-2,2-dimethyl-3-phenyl-4-chromanyl)phenoxy]ethyl]-, trans- (8CI)
OTHER NAMES:
CN 1-[2-[p-(trans-7-Methoxy-2,2-dimethyl-3-phenyl-4-chromanyl)phenoxy]ethyl]pyrrolidine
CN 67/20
CN **Centchroman**
CN Ormeloxifene
CN trans-Centchroman
FS STEREOSEARCH
DR 78994-24-8
MF C30 H35 N O3
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CIN, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Relative stereochemistry.



129 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
129 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> e raloxifen/cn

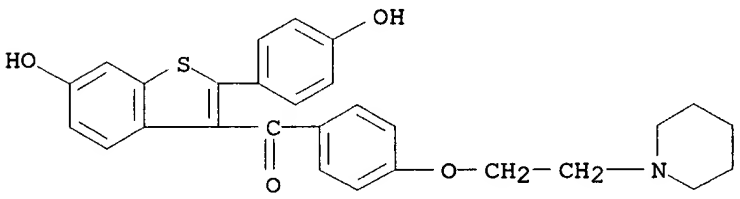
E1	1	RALOX BHT/CN
E2	1	RALOX LC/CN
E3	0 -->	RALOXIFEN/CN
E4	1	RALOXIFENE/CN
E5	1	RALOXIFENE HYDROCHLORIDE/CN
E6	3	RALSTONITE/CN
E7	1	RALSTONITE (ALF2(OH))/CN
E8	1	RALSTONITE (ALF2(OH).1/2H2O)/CN
E9	1	RALTITREXED/CN
E10	1	RALUBEN/CN
E11	1	RALUFON DCH/CN
E12	1	RALUFON DL/CN

=> s e4

L2 1 RALOXIFENE/CN

=> d l2 1

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1999 ACS
RN 84449-90-1 REGISTRY
CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Keoxifene
CN LY 139481
CN **Raloxifene**
CN [2-(4-Hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-(2-(1-piperidinyl)ethoxy)phenyl]methanone
FS 3D CONCORD
MF C28 H27 N O4 S
CI COM
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CBNB, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



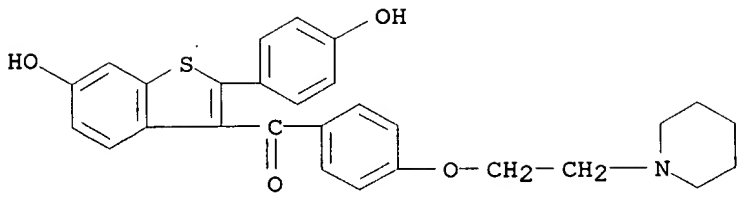
275 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
275 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s e5

L3 1 "RALOXIFENE HYDROCHLORIDE"/CN

=> d l3 1

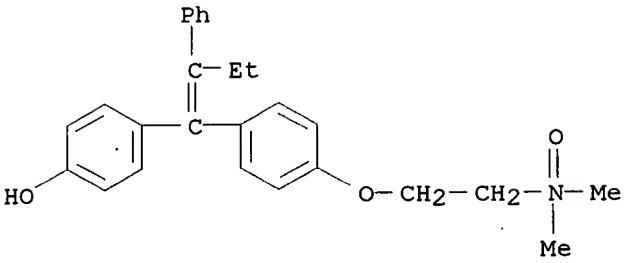
L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1999 ACS
RN 82640-04-8 REGISTRY
CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]-, hydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN LY 156758
CN **Raloxifene hydrochloride**
MF C28 H27 N O4 S . Cl H
CI COM
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CIN, DRUGPAT, DRUGUPDATES, EMBASE, IPA, MRCK*, PHAR, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
CRN (84449-90-1)



● HCl

161 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
161 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
=> e droloxifen/cn

E1            1     DROLBAN/CN
E2            1     DROLEPTAN/CN
E3            0 --> DROLOXIFEN/CN
E4            1     DROLOXIFENE/CN
E5            1     DROLOXIFENE CITRATE/CN
E6            1     DROLOXIFENE N-OXIDE/CN
E7            1     DROLUENE 10/CN
E8            1     DROLUENE 2.5/CN
E9            1     DROLUENE 25/CN
E10           1     DROLUENE 5/CN
E11           1     DROME PROTEIN (ILE-149) (HUMAN CLONE PBL-2)/CN
E12           1     DROME PROTEIN (MET-149) (HUMAN CLONE PBL-2)/CN

=> s (e4 or e5 or e6)

              1 DROLOXIFENE/CN
              1 "DROLOXIFENE CITRATE"/CN
              1 "DROLOXIFENE N-OXIDE"/CN
L4            3 (DROLOXIFENE/CN OR "DROLOXIFENE CITRATE"/CN OR "DROLOXIFENE
                N-OXIDE"/CN)

=> d l4 1-3


L4   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 1999 ACS
RN   110025-26-8  REGISTRY
CN   Phenol,
4-[1-[4-[2-(dimethyloxidoamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Phenol, 4-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-,
     N-oxide
OTHER NAMES:
CN   Droloxifene N-oxide
FS   3D CONCORD
MF   C26 H29 N O3
SR   CA
LC   STN Files:   CA, CAPLUS, TOXLIT
```



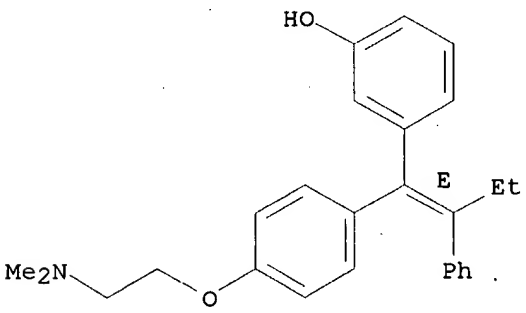
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 2 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN 97752-20-0 REGISTRY
CN Phenol,
3-[(1E)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-
, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, 3-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-, (E)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt)
OTHER NAMES:
CN **Droloxifene citrate**
FS STEREOSEARCH
MF C26 H29 N O2 . C6 H8 O7
SR Commission of European Communities
LC STN Files: BIOSIS, CA, CAPLUS, CHEMLIST, DRUGPAT, DRUGUPDATES, MRCK*, PROMT, RTECS*, TOXLIT, ULIDAT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

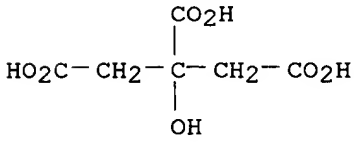
CRN 82413-20-5
CMF C26 H29 N O2

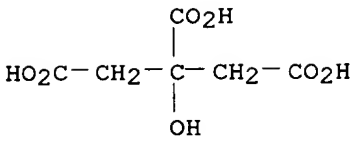
Double bond geometry as shown.



CM 2

CRN 77-92-9
CMF C6 H8 O7

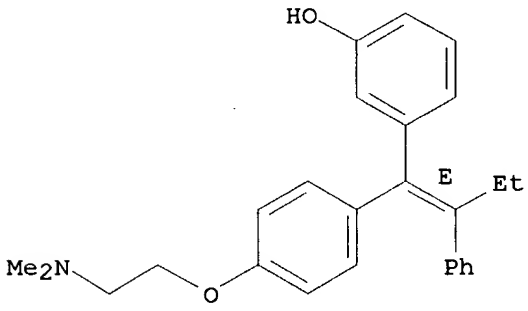




24 REFERENCES IN FILE CA (1967 TO DATE)
24 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 3 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN 82413-20-5 REGISTRY
CN Phenol,
3-[(1E)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, 3-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-,
(E)-
OTHER NAMES:
CN 3-Hydroxytamoxifen
CN **Droloxifene**
CN E-Droloxifene
CN K 060
CN K 060E
CN K 21.060E
FS STEREOSEARCH
MF C26 H29 N O2
CI COM
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGNL,
DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT,
RTECS*, TOXLINE, TOXLIT, ULIDAT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Double bond geometry as shown.



110 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
110 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 17:02:10 ON 15 JUL 1999)

FILE 'REGISTRY' ENTERED AT 17:02:42 ON 15 JUL 1999
E RALOXIFEN/CN
E DROLOXIFEN/CN
E CENTCHROMAN/CN
L1 1 S E3

```
                E RALOXIFEN/CN
L2            1 S E4
L3            1 S E5
                E DROLOXIFEN/CN
L4            3 S (E4 OR E5 OR E6)

=> file caplus, uspatfull, medline, biosis
```

```
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FILE 'MEDLINE' ENTERED AT 17:06:30 ON 15 JUL 1999

FILE 'BIOSIS' ENTERED AT 17:06:30 ON 15 JUL 1999
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=> s (l1 or l2 or l3 or l4)

L5         1460 (L1 OR L2 OR L3 OR L4)

=> s (LHRH OR LUTEIN?(W)HORMONE#(W)RELEAS?(W)HORMONE#)

L6        31888 (LHRH OR LUTEIN?(W) HORMONE#(W) RELEAS?(W) HORMONE#)

=> s l5 and l6

L7           21 L5 AND L6

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8            17 DUP REM L7 (4 DUPLICATES REMOVED)

=> d l8 abs ibib kwic 1-17
```

```
FILE 'HOME' ENTERED AT 15:15:18 ON 15 JUL 1999

=> file caplus, uspatfull, medline, biosis

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

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FILE 'USPATFULL' ENTERED AT 15:15:32 ON 15 JUL 1999
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FILE 'MEDLINE' ENTERED AT 15:15:32 ON 15 JUL 1999

FILE 'BIOSIS' ENTERED AT 15:15:32 ON 15 JUL 1999
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=> s (endometrio? or myoma?)

L1       22402 (ENDOMETRIO? OR MYOMA?)

=> s (lhrh or zoladex or ramorelix or buserelin or antide or cetrorelix)

L2       29052 (LHRH OR ZOLADEX OR RAMORELIX OR BUSERELIN OR ANTIDE OR
CETROREL
               IX)

=> s l1 and l2

L3         877 L1 AND L2

=> s l1(p)l2

L4         548 L1(P) L2

=> s (tamoxifen or raloxifen or droloxifen or centchroman)

L5       21743 (TAMOXIFEN OR RALOXIFEN OR DROLOXIFEN OR CENTCHROMAN)

=> s l4 and l5

L6           5 L4 AND L5

=> dup rem l6

PROCESSING COMPLETED FOR L6
L7             4 DUP REM L6 (1 DUPLICATE REMOVED)

=> d l7 abs ibib kwic 1-4


L7   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 1999 ACS
AB   Combinations of LH-RH analogs and antiestrogens with tissue-selective
     estrogenic activity are useful for treatment of gynecol. disorders, esp.
     endometriosis and myomas.  Thus, in rats with i.p.
```

implants of endometrium as a model of **endometriosis**, the LH-RH antagonist **antide** (0.5 mg s.c. every 3 days for 4 wk) produced complete regression of cystic foci of **endometriosis**, but simultaneously to a redn. in endogenous estrogen level resembling that occurring after ovariectomy, with a decrease in bone d. and an increase in osteoclast activity. When the antiestrogen **raloxifen** (3 mg/day orally) was also administered during the period of **antide** administration, the **endometriosis** regressed but no decrease in estrogen level occurred.

ACCESSION NUMBER: 1997:543582 CAPLUS
DOCUMENT NUMBER: 127:140580
TITLE: Combination of LH-RH analogs and antiestrogens for treatment of gynecological disorders
INVENTOR(S): Stoeckemann, Klaus; Muhn, Peter
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19604231	A1	19970731	DE 96-19604231	19960129
WO 9727863	A1	19970807	WO 97-EP395	19970129
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9715969	A1	19970822	AU 97-15969	19970129
EP 877621	A1	19981118	EP 97-902258	19970129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1209750	A	19990303	CN 97-191940	19970129
NO 9803465	A	19980918	NO 98-3465	19980728
PRIORITY APPLN. INFO.:			DE 96-19604231	19960129
			WO 97-EP395	19970129

AB Combinations of LH-RH analogs and antiestrogens with tissue-selective estrogenic activity are useful for treatment of gynecol. disorders, esp. **endometriosis** and **myomas**. Thus, in rats with i.p. implants of endometrium as a model of **endometriosis**, the LH-RH antagonist **antide** (0.5 mg s.c. every 3 days for 4 wk) produced complete regression of cystic foci of **endometriosis**, but simultaneously to a redn. in endogenous estrogen level resembling that occurring after ovariectomy, with a decrease in bone d. and an increase in osteoclast activity. When the antiestrogen **raloxifen** (3 mg/day orally) was also administered during the period of **antide** administration, the **endometriosis** regressed but no decrease in estrogen level occurred.

ST **LHRH** analog antiestrogen **endometriosis** treatment; **antide raloxifen endometriosis** treatment; **myoma** treatment **LHRH** analog antiestrogen; gynecol disorder **LHRH** analog antiestrogen

IT 9034-40-6D, LHRH, analogs 31477-60-8, **Centchroman** 53714-56-0, Leuprorelin 57982-77-1 65807-02-5, Zoladex 82413-20-5, Droloxifene 84449-90-1, Raloxifene 112568-12-4, Antide 120287-85-6, Cetrorelix 127932-90-5, Ramorelix 193147-32-9
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of LH-RH analogs and antiestrogens for treatment of

gynecol. disorders)

L7 ANSWER 2 OF 4 BIOSIS COPYRIGHT 1999 BIOSIS
AB **Tamoxifen** used for adjuvant therapy in breast cancer, has a complex and unclear action on endometrium and myometrium. Many authors demonstrated endometrial proliferous changes in peri and post menopausal women. Our study shows the development of **myomas** in three patients without uterine pathology before **tamoxifen** therapy, and the increase of a polyp and a **myoma** after **tamoxifen** therapy. Moreover, we observed the development of a **myoma** in a patient after one year **tamoxifen** in association with **LHRH** analogue therapy. It is necessary to continue our study with a larger number of patients to assess the hyperplasia effect of **tamoxifen**.
ACCESSION NUMBER: 1993:345129 BIOSIS
DOCUMENT NUMBER: PREV199396042129
TITLE: Uterine changes during **tamoxifen** therapy.
AUTHOR(S): Rullo, S.; Tagliaferri, T.; Bandiera, F.; Fiorelli, C.; Felici, A.; Piccioni, M. G.; Framarino Dei Malatesta, M. L.
(1)
CORPORATE SOURCE: (1) III Clin. Osterica Ginecol., Univ. di Roma "La Sapienza", Policlin. Umberto I, 00161 Roma Italy
SOURCE: Clinical and Experimental Obstetrics & Gynecology, (1993) Vol. 20, No. 2, pp. 116-119.
ISSN: 0390-6663.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Uterine changes during **tamoxifen** therapy.
AB **Tamoxifen** used for adjuvant therapy in breast cancer, has a complex and unclear action on endometrium and myometrium. Many authors demonstrated endometrial proliferous changes in peri and post menopausal women. Our study shows the development of **myomas** in three patients without uterine pathology before **tamoxifen** therapy, and the increase of a polyp and a **myoma** after **tamoxifen** therapy. Moreover, we observed the development of a **myoma** in a patient after one year **tamoxifen** in association with **LHRH** analogue therapy. It is necessary to continue our study with a larger number of patients to assess the hyperplasia effect of **tamoxifen**.
IT Major Concepts
Development; Oncology (Human Medicine, Medical Sciences); Pharmacology;
Reproductive System (Reproduction); Toxicology
IT Chemicals & Biochemicals
TAMOXIFEN
RN 10540-29-1 (**TAMOXIFEN**)

L7 ANSWER 3 OF 4 MEDLINE DUPLICATE 1
AB In young women chronic use of luteinizing hormone releasing hormone (**LHRH**) agonists such as **buserelin** to treat **endometriosis** leads to estrogen-deficiency bone loss. **Tamoxifen** citrate is an estrogen agonist/antagonist which protects the skeleton from osteopenia when ovarian hormones are depleted. The present study was undertaken to determine whether **tamoxifen** citrate (20 mg/kg body wt/week s.c.) could prevent the osteopenic effect of **buserelin** (25 micrograms/kg body wt/day s.c.). Four groups of rats with 45Ca-labelled bones were studied for 4 weeks: group A--placebo controls; group B--**buserelin**; Group C--**tamoxifen**; group D--**buserelin+tamoxifen**. Bone resorption was monitored by measuring the urinary excretion of 45Ca and hydroxyproline. Interestingly **buserelin** lowered both blood 17 beta-estradiol values and uterine weights in the presence and absence of **tamoxifen**. However, **tamoxifen** slowed bone breakdown and inhibited the bone-thinning effects of **buserelin**. Total body calcium values (mg; means +/- S.D.) were: 2227 +/- 137; 1926 +/- 124;

+/- 94 and 2268 +/- 163, in groups A to D respectively. Osteopenia was thus present only in group B (P less than 0.001). Because **tamoxifen** inhibits estrogen-deficiency bone loss in **buserelin**-treated rats without depressing the hypoestrogenic actions of this **LHRH**-agonist, we suggest that use of **tamoxifen** to protect the skeleton during **LHRH**-agonist therapy in young women should be explored. **Tamoxifen** citrate might also help to prevent postmenopausal osteoporosis.

ACCESSION NUMBER: 92404819 MEDLINE
DOCUMENT NUMBER: 92404819
TITLE: **Tamoxifen** in the rat prevents estrogen-deficiency bone loss elicited with the LHRH agonist buserelin.
AUTHOR: Goulding A; Gold E; Feng W
CORPORATE SOURCE: Department of Medicine, University of Otago Medical School,
Dunedin, New Zealand..
SOURCE: BONE AND MINERAL, (1992 Aug) 18 (2) 143-52.
Journal code: BMI. ISSN: 0169-6009.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212

TI **Tamoxifen** in the rat prevents estrogen-deficiency bone loss elicited with the LHRH agonist buserelin.

AB In young women chronic use of luteinizing hormone releasing hormone (**LHRH**) agonists such as **buserelin** to treat **endometriosis** leads to estrogen-deficiency bone loss. **Tamoxifen** citrate is an estrogen agonist/antagonist which protects the skeleton from osteopenia when ovarian hormones are depleted. The present study was undertaken to determine whether **tamoxifen** citrate (20 mg/kg body wt/week s.c.) could prevent the osteopenic effect of **buserelin** (25 micrograms/kg body wt/day s.c.). Four groups of rats with 45Ca-labelled bones were studied for 4 weeks: group A--placebo controls; group B--**buserelin**; Group C--**tamoxifen**; group D--**buserelin**+**tamoxifen**. Bone resorption was monitored by measuring the urinary excretion of 45Ca and hydroxyproline. Interestingly **buserelin** lowered both blood 17 beta-estradiol values and uterine weights in the presence and absence of **tamoxifen**. However, **tamoxifen** slowed bone breakdown and inhibited the bone-thinning effects of **buserelin**. Total body calcium values (mg; means +/- S.D.) were: 2227 +/- 137; 1926 +/- 124; 2233
+/- 94 and 2268. . . 163, in groups A to D respectively. Osteopenia was
thus present only in group B (P less than 0.001). Because **tamoxifen** inhibits estrogen-deficiency bone loss in **buserelin**-treated rats without depressing the hypoestrogenic actions of this **LHRH**-agonist, we suggest that use of **tamoxifen** to protect the skeleton during **LHRH**-agonist therapy in young women should be explored. **Tamoxifen** citrate might also help to prevent postmenopausal osteoporosis.

CT . . .

BL, blood
*Estrogens: DF, deficiency
Gonadorelin: ME, metabolism
Hydroxyproline: UR, urine
Organ Weight: DE, drug effects
Rats
Rats, Inbred Strains
***Tamoxifen: PD, pharmacology**
Uterus: DE, drug effects

RN **10540-29-1 (Tamoxifen)**; 33515-09-2 (Gonadorelin); 50-28-2 (Estradiol); 51-35-4 (Hydroxyproline); 57982-77-1 (Buserelin); 7440-70-2 (Calcium)

L7 ANSWER 4 OF 4 BIOSIS COPYRIGHT 1999 BIOSIS

AB The effect of medical oophorectomy induced by treatment with the luteinizing hormone-releasing hormone (LH-RH) agonist[D-Trp6,des-Gly-NH210]LH-RH ethylamide was studied in 34 patients with laparoscopically proven endometriosis. **Tamoxifen** was administered during the 1st month of therapy to prevent flare-up of the disease during the estrogen surge. Fifteen women had a decrease of their laparoscopy scores translated into an improvement in the stage of disease, whereas in 12 others, the decrease in their scores was not enough to allow a change of disease stage. The 2nd laparoscopy was not performed in 7 women. Medical oophorectomy, after daily injection of the LH-RH agonist (LH-RH-a), was accompanied by low levels of circulating estradiol. The serum concentration of all .DELTA.4-3-ketosteroids was significantly decreased during medical oophorectomy, whereas the level of circulating .DELTA.5-3.beta.-hydroxysteroids was not altered except for pregnenolone. The present data indicate that medical oophorectomy induced by an LH-RH-a in association with **tamoxifen** is a very efficient and well tolerated therapy in endometriosis.

ACCESSION NUMBER: 1990:452916 BIOSIS
DOCUMENT NUMBER: BA90:103556
TITLE: HORMONAL AND BIOCHEMICAL CHANGES DURING TREATMENT OF **ENDOMETRIOSIS** WITH THE LUTEINIZING HORMONE-RELEASING HORMONE **LHRH** AGONIST D TRP-6 DES-GLY-AMIDE-10 **LHRH** ETHYLAMIDE.
AUTHOR(S): DUPONT A; DUPONT P; BELANGER A; MAILOUX J; CUSAN L; LABRIE F
CORPORATE SOURCE: LAB. MOL. ENDOCRINOL., CHUL RES. CENT., 2705 LAURIER BLVD., QUEBEC G1V 4G2, QUEBEC, CANADA.
SOURCE: FERTIL STERIL, (1990) 54 (2), 227-232.
CODEN: FESTAS. ISSN: 0015-0282.
FILE SEGMENT: BA; OLD
LANGUAGE: English

TI HORMONAL AND BIOCHEMICAL CHANGES DURING TREATMENT OF **ENDOMETRIOSIS** WITH THE LUTEINIZING HORMONE-RELEASING HORMONE **LHRH** AGONIST D TRP-6 DES-GLY-AMIDE-10 **LHRH** ETHYLAMIDE.

AB. . . induced by treatment with the luteinizing hormone-releasing hormone (LH-RH) agonist[D-Trp6,des-Gly-NH210]LH-RH ethylamide was studied in 34 patients with laparoscopically proven endometriosis. **Tamoxifen** was administered during the 1st month of therapy to prevent flare-up of the disease during the estrogen surge. Fifteen women. . . was not altered except for pregnenolone. The present data indicate that medical oophorectomy induced by an LH-RH-a in association with **tamoxifen** is a very efficient and well tolerated therapy in endometriosis.

IT Miscellaneous Descriptors
HUMAN DECAPEPTYL **TAMOXIFEN** METABOLIC-DRUG ESTRADIOL INFERTILITY OOPHORECTOMY

RN 50-28-2 (ESTRADIOL)
9002-67-9 (LUTEINIZING HORMONE)
9034-40-6 (LHRH)
10540-29-1 (**TAMOXIFEN**)
57773-63-4 (DECAPEPTYL)

=> d his

(FILE 'HOME' ENTERED AT 15:15:18 ON 15 JUL 1999)

FILE 'CAPLUS, USPATFULL, MEDLINE, BIOSIS' ENTERED AT 15:15:32 ON 15 JUL 1999

L1 22402 S (ENDOMETRIO? OR MYOMA?)
L2 29052 S (LHRH OR ZOLADEX OR RAMORELIX OR BUSERELIN OR ANTIDE OR CETRO
L3 877 S L1 AND L2

```
L4          548 S L1(P)L2
L5        21743 S (TAMOXIFEN OR RALOXIFEN OR DROLOXIFEN OR CENTCHROMAN)
L6            5 S L4 AND L5
L7            4 DUP REM L6 (1 DUPLICATE REMOVED)

=> s l3 and l5

L8           40 L3 AND L5

=> dup rem l8

PROCESSING COMPLETED FOR L8
L9           39 DUP REM L8 (1 DUPLICATE REMOVED)
```

=> s l9 and py <=1997

   3 FILES SEARCHED...
L10   24 L9 AND PY <=1997

=> d l10 abs ibib kwic 1-24

L10 ANSWER 1 OF 24 CAPLUS COPYRIGHT 1999 ACS
AB Combinations of LH-RH analogs and antiestrogens with tissue-selective estrogenic activity are useful for treatment of gynecol. disorders, esp. **endometriosis** and **myomas**. Thus, in rats with i.p. implants of endometrium as a model of **endometriosis**, the LH-RH antagonist **antide** (0.5 mg s.c. every 3 days for 4 wk) produced complete regression of cystic foci of **endometriosis**, but simultaneously to a redn. in endogenous estrogen level resembling that occurring after ovariectomy, with a decrease in bone d. and an increase in osteoclast activity. When the antiestrogen **raloxifen** (3 mg/day orally) was also administered during the period of **antide** administration, the **endometriosis** regressed but no decrease in estrogen level occurred.

ACCESSION NUMBER: 1997:543582 CAPLUS
DOCUMENT NUMBER: 127:140580
TITLE: Combination of LH-RH analogs and antiestrogens for treatment of gynecological disorders
INVENTOR(S): Stoeckemann, Klaus; Muhn, Peter
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 19604231	A1	19970731	DE 96-19604231	19960129	<--
WO 9727863	A1	19970807	WO 97-EP395	19970129	<--
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9715969	A1	19970822	AU 97-15969	19970129	<--
EP 877621	A1	19981118	EP 97-902258	19970129	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1209750	A	19990303	CN 97-191940	19970129	
NO 9803465	A	19980918	NO 98-3465	19980728	
PRIORITY APPLN. INFO.:			DE 96-19604231	19960129	
			WO 97-EP395	19970129	

PI DE 19604231 A1 **19970731**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI DE 19604231	A1	19970731	DE 96-19604231	19960129	<--
WO 9727863	A1	19970807	WO 97-EP395	19970129	<--

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9715969	A1	19970822	AU 97-15969	19970129 <--
EP 877621	A1	19981118	EP 97-902258	19970129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1209750	A	19990303	CN 97-191940	19970129
NO 9803465	A	19980918	NO 98-3465	19980728

AB Combinations of LH-RH analogs and antiestrogens with tissue-selective estrogenic activity are useful for treatment of gynecol. disorders, esp. **endometriosis** and **myomas**. Thus, in rats with i.p. implants of endometrium as a model of **endometriosis**, the LH-RH antagonist **antide** (0.5 mg s.c. every 3 days for 4 wk) produced complete regression of cystic foci of **endometriosis**, but simultaneously to a redn. in endogenous estrogen level resembling that occurring after ovariectomy, with a decrease in bone d. and an increase in osteoclast activity. When the antiestrogen **raloxifen** (3 mg/day orally) was also administered during the period of **antide** administration, the **endometriosis** regressed but no decrease in estrogen level occurred.

ST **LHRH** analog antiestrogen **endometriosis** treatment; **antide raloxifen endometriosis** treatment; **myoma** treatment **LHRH** analog antiestrogen; gynecol disorder **LHRH** analog antiestrogen

IT **Endometriosis**
Myoma
(combination of LH-RH analogs and antiestrogens for treatment of gynecol. disorders)

IT 9034-40-6D, **LHRH**, analogs 31477-60-8, **Centchroman** 53714-56-0, Leuprorelin 57982-77-1 65807-02-5, **Zoladex** 82413-20-5, Droloxifene 84449-90-1, Raloxifene 112568-12-4, **Antide** 120287-85-6, **Cetrorelix** 127932-90-5, **Ramorelix** 193147-32-9
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of LH-RH analogs and antiestrogens for treatment of gynecol. disorders)

L10 ANSWER 2 OF 24 CAPLUS COPYRIGHT 1999 ACS

AB Since uterine leiomyomata (fibroids) are not found in conditions where estradiol is either absent or present only in low concns., estradiol is considered to be an important factor in the control of fibroid growth. To detn. whether this is due to a direct effect on the tissue, estradiol and progesterone receptors were measured in tissue removed at hysterectomy from normally cycling women, women who had received the gonadotropin-releasing hormone (GnRH) agonist **Zoladex** (ICI 118630) as a s.c. depot given at monthly intervals for 3 mo preoperatively, and women who had received the antiestrogen **tamoxifen** (20 mg daily) for 3 mo before surgery. Both unoccupied estradiol receptors (measured by sepg. bound from free hormone with dextran-coated charcoal) and total receptor populations (as measured by an enzyme immunoassay) were measured in each fibroid and adjoining myometrium. There was more binding of both estradiol and progestogen to fibroid than to myometrium in both the control and agonist-treated groups.
Estradiol binding to fibroids in women treated with **Zoladex** exceeded that in the normally cycling women which in turn exceeded that in

the **tamoxifen**-treated group. However, the binding of progestogen, measured by dextran-coated charcoal, showed the reverse trend. These results may be explained by the low circulating estradiol concn. in the GnRH agonist-treated women, leading to low receptor occupancy.

ACCESSION NUMBER: 1989:206008 CAPLUS
DOCUMENT NUMBER: 110:206008
TITLE: The binding of steroids to myometrium and leiomyomata (fibroids) in women treated with the gonadotropin-releasing hormone agonist **Zoladex** (ICI 118630)
AUTHOR(S): Lumsden, M. A.; West, C. P.; Hawkins, R. A.; Bramley, T. A.; Rumgay, L.; Baird, D. T.
CORPORATE SOURCE: Cent. Reprod. Biol., Univ. Edinburgh, Edinburgh, EH3 9EW, UK
SOURCE: J. Endocrinol. (**1989**), 121(2), 389-96
CODEN: JOENAK; ISSN: 0022-0795
DOCUMENT TYPE: Journal
LANGUAGE: English

TI The binding of steroids to myometrium and leiomyomata (fibroids) in women treated with the gonadotropin-releasing hormone agonist **Zoladex** (ICI 118630)

SO J. Endocrinol. (**1989**), 121(2), 389-96
CODEN: JOENAK; ISSN: 0022-0795

AB . . . were measured in tissue removed at hysterectomy from normally cycling women, women who had received the gonadotropin-releasing hormone (GnRH) agonist **Zoladex** (ICI 118630) as a s.c. depot given at monthly intervals for 3 mo preoperatively, and women who had received the antiestrogen **tamoxifen** (20 mg daily) for 3 mo before surgery. Both unoccupied estradiol receptors (measured by sepg. bound from free hormone with. . . to fibroid than to myometrium in both the control and agonist-treated groups. Estradiol binding to fibroids in women treated with **Zoladex** exceeded that in the normally cycling women which in turn exceeded that in the **tamoxifen**-treated group. However, the binding of progestogen, measured by dextran-coated charcoal, showed the reverse trend. These results may be explained by. . .

ST leiomyomata steroid receptor; **LHRH** agonist uterus steroid receptor

IT **Myoma**
(leio-, estradiol and progestogen receptors of, in women, gonadotropin-releasing hormone agonist effect on)

IT 65807-02-5, **Zoladex**
RL: BIOL (Biological study)
(steroid receptors of uterus response to, in women)

L10 ANSWER 3 OF 24 USPATFULL

AB Inhibitors of sex steroid activity, for example those having the general structure ##STR1## may be used as part of a pharmaceutical composition to provide antiestrogenic effects and/or to suppress estrogen synthesis. Such pharmaceutical compositions are useful for the treatment of breast cancer or other diseases whose progress is aided by activation of sex steroid receptors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:104491 USPATFULL
TITLE: Sex steroid activity inhibitors
INVENTOR(S): Labrie, Fernand, Quebec, Canada
Merand, Yves, Quebec, Canada
PATENT ASSIGNEE(S): Endorecherche Inc., Quebec, Canada (non-U.S. corporation)

NUMBER	DATE

PATENT INFORMATION: US 5686465 19971111 <--
APPLICATION INFO.: US 95-485739 19950607 (8)
RELATED APPLN. INFO.: Division of Ser. No. US 94-285354, filed on 3 Aug 1994 which is a division of Ser. No. US 91-801704, filed on 2 Dec 1991, now patented, Pat. No. US 5395842 which is a continuation-in-part of Ser. No. US 89-377010, filed on 7 Jul 1989, now abandoned And Ser. No. US 88-265150, filed on 31 Oct 1988, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen, LLP
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 3210
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5686465 19971111 <--
SUMM H. Mouridsen et al., Cancer Treatm. Rev. 5: 131-141 (1978), discloses that **Tamoxifen**, an antiestrogen, is effective in remission of advanced breast cancer in about 30 percent of the women patients treated.
SUMM The combined use of the antiestrogen **Tamoxifen** and a luteinizing hormone-releasing hormone agonist, **Buserelin**, is also known for treatment of breast cancer. See, for instance, Klijn et al. J. Steroid Biochem. 420: no. 6B,. . .
SUMM . . . male animals including humans whose testicular hormonal secretions are blocked by surgical or chemical means, e.g., by use of an **LHRH** agonist, e.g., [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10] **LHRH** ethylamide. The treatment includes administering an antiandrogen, e.g., flutamide in association with at least one inhibitor of sex steroid biosynthesis,. . .
SUMM U.S. Pat. No. 4,472,382 relates to a method of treating prostate cancer using the combination of an antiandrogen and an **LHRH** agonist.
SUMM . . . in the treatment of estrogen-related diseases. These diseases include, but are not limited to breast cancer, uterine cancer, ovarian cancer, **endometriosis**, uterine fibroma, precocious puberty and benign prostatic hyperplasia.
DETD When administered systemically, pharmaceuticals of the inventions may be used in the treatment of breast cancer, uterine cancer, ovarian cancer, **endometriosis**, uterine fibroma, precocious puberty and benign prostatic hyperplasia.

L10 ANSWER 4 OF 24 USPATFULL
AB The present invention relates to a purified, easily produced poly-.beta.-1.fwdarw.4-N-acetylglucosamine (p-GlcNAc) polysaccharide species useful in collagen copolymers. The p-GlcNAc of the invention is a polymer of high molecular weight whose constituent monosaccharide sugars are attached in a .beta.-1.fwdarw.4 conformation, and which is free of proteins, and substantially free of single amino acids, and other organic and inorganic contaminants. In addition, derivatives and reformulations of p-GlcNAc are described. The present invention further relates to methods for the purification of the p-GlcNAc of the invention from microalgae, preferably diatom, starting sources. Still further, the invention relates to methods for the derivatization and reformulation of the p-GlcNAc. Additionally, the present invention relates to the uses of pure p-GlcNAc, its derivatives, and/or its reformulations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:104147 USPATFULL
TITLE: Poly-.beta.-1.fwdarw.4-N-acetylucosamine copolymer composition with collagen
INVENTOR(S): Vournakis, John N., Hanover, NH, United States
Finkielsztein, Sergio, Chestnut Hill, MA, United States
Pariser, Ernest R., Belmont, MA, United States
Helton, Mike, Memphis, TN, United States
PATENT ASSIGNEE(S): Marine Polymer Technologies, Inc., Danvers, MA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5686115	19971111	<--
APPLICATION INFO.:	US 95-470912	19950606 (8)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 94-347911, filed on 1 Dec 1994, now patented, Pat. No. US 5623064 which is a continuation-in-part of Ser. No. US 93-160569, filed on 1 Dec 1993, now patented, Pat. No. US 5622834
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Kight, John
ASSISTANT EXAMINER: Fonda, Kathleen Kahler
LEGAL REPRESENTATIVE: Pennie & Edmonds
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 72 Drawing Figure(s); 58 Drawing Page(s)
LINE COUNT: 4073
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5686115 19971111 <--
DETD . . . (ara-C) are contemplated for use in the invention as an improved treatment for acute nonlymphocytic leukemia. Other synergistic combinations include **tamoxifen** with cisplatin for breast cancer, and prostaglandins with cisplatin for breast and prostate cancer. Additionally, many other synergistic combinations of. . .
DETD . . . prednisolone and dexamethasone), estrogens, (diethylstibesterol, estradiol, esterified estrogens, conjugated estrogen, chlorotiasnene), progestins (medroxyprogesterone acetate, hydroxy progesterone caproate, megestrol acetate), antiestrogens (**tamoxifen**), aromastase inhibitors (aminoglutethimide), androgens (testosterone propionate, methyltestosterone, fluoxymesterone, testolactone), antiandrogens (flutamide), **LHRH** analogues (leuprolide acetate), and endocrines for prostate cancer (ketoconazole).
DETD . . . in trauma wounds, for example, spleen, liver and blood vessel injuries; in standard and minimally invasive surgical procedures, for example, **endometriosis** surgery and operations on the gallbladder; in soft and hard tissue wound repair, for example, skin wounds and burn healing;. . .

L10 ANSWER 5 OF 24 USPATFULL
AB The present invention relates to a purified, easily produced poly-.beta.-1.fwdarw.4-N-acetylglucosamine (p-GlcNAc) polysaccharide species useful in drug compositions. The p-GlcNAc of the invention is a polymer of high molecular weight whose constituent monosaccharide sugars are attached in a .beta.-1.fwdarw.4 conformation, and which is free of proteins, and substantially free of single amino acids, and other organic and inorganic contaminants. In addition, derivatives and reformulations of p-GlcNAc are described. The present invention further relates to methods for the purification of the p-GlcNAc of the invention from microalgae, preferably diatom, starting sources. Still further, the invention relates to methods for the derivatization and reformulation of

the p-GlcNAc. Additionally, the present invention relates to the uses of
pure p-GlcNAc, its derivatives, and/or its reformulations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	97:47398 USPATFULL
TITLE:	Methods and compositions for poly-.beta.-1-4-N-acetylglucosamine chemotherapeutics
INVENTOR(S):	Vournakis, John N., Hanover, NH, United States Finkielsztein, Sergio, Chestnut Hill, MA, United States Pariser, Ernest R., Belmont, MA, United States Helton, Mike, Memphis, TN, United States
PATENT ASSIGNEE(S):	Marine Polymer Technologies, Inc., Danvers, MA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5635493	19970603	<--
APPLICATION INFO.:	US 95-471545	19950606 (8)	
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 94-347911, filed on 1 Dec 1994 which is a continuation-in-part of Ser. No. US 93-160569, filed on 1 Dec 1993		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Kight, John		
ASSISTANT EXAMINER:	Fonda, Kathleen Kahler		
LEGAL REPRESENTATIVE:	Pennie & Edmonds		
NUMBER OF CLAIMS:	16		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	73 Drawing Figure(s); 58 Drawing Page(s)		
LINE COUNT:	3937		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5635493 19970603 <--

DETD . . . (ara-C) are contemplated for use in the invention as an improved treatment for acute nonlymphocytic leukemia. Other synergistic combinations include **tamoxifen** with cisplatin for breast cancer, and prostaglandins with cisplatin for breast and prostate cancer. Additionally, many other synergistic combinations of. . .

DETD . . . prednisolone and dexamethasone), estrogens, (diethylstibesterol, estradiol, esterified estrogens, conjugated estrogen, chlorotiasnene), progestins (medroxyprogesterone acetate, hydroxy progesterone caproate, megestrol acetate), antiestrogens (**tamoxifen**), aromastase inhibitors (aminoglutethimide), androgens (testosterone propionate, methyltestosterone, fluoxymesterone, testolactone), antiandrogens (flutamide), **LHRH** analogues (leuprolide acetate), and endocrines for prostate cancer (ketoconazole).

DETD . . . in trauma wounds, for example, spleen, liver and blood vessel injuries; in standard and minimally invasive surgical procedures, for example, **endometriosis** surgery and operations on the gallbladder; in soft and hard tissue wound repair, for example, skin wounds and burn healing;. . .

L10 ANSWER 6 OF 24 USPATFULL

AB Certain toxic compounds (T) such as, for example, compounds based upon diphtheria toxin, ricin toxin, pseudomonas exotoxin, .alpha.-amanitin, pokeweed antiviral protein (PAP), ribosome inhibiting proteins, especially the ribosome inhibiting proteins of barley, wheat, corn, rye, gelonin and abrin, as well as certain cytotoxic chemicals such as, for example, melphalan and daunomycin can be conjugated to certain analogs of gonadotropin-releasing hormone to form a class of compounds which, when injected into an animal, destroy the gonadotrophs of the animal's anterior pituitary gland. Hence such compounds may be used to sterilize such animals and/or to treat certain sex hormone related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 97:42855 USPATFULL
TITLE: Method for inactivating gonadotrophs
INVENTOR(S): Nett, Torrance M., Ft. Collins, CO, United States
Glode, Leonard M., Aurora, CO, United States
PATENT ASSIGNEE(S): Colorado State University Research Foundation, Fort Colllins, CO, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5631229	19970520	<--
APPLICATION INFO.:	US 93-88434	19930707 (8)	

RELATED APPLN. INFO.: Division of Ser. No. US 92-837639, filed on 14 Feb 1992, now patented, Pat. No. US 5378688 which is a continuation-in-part of Ser. No. US 89-314653, filed on
23 Feb 1989, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Davenport, Avis M.
LEGAL REPRESENTATIVE: Sheridan Ross & McIntosh
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1459
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5631229 19970520 <--
SUMM . . . of the steroidal hormones, estradiol, progesterone and testosterone. It should also be noted that the terms "GnRH" (gonadotropin-releasing hormone) and "**LHRH**" (luteinizing hormone-releasing hormone) are sometimes used interchangeably in the literature. For the purposes of describing the prior art both terms. .
.
SUMM . . . regard was recently published in the INTERNATIONAL JOURNAL OF PHARMACOLOGY 76: R5-R8 by Singh et al. entitled "Controlled release of **LHRH**-DT from bioerodible hydrogel microspheres." Generally speaking, it teaches that a natural GnRH/diphtheria toxin can be used as
a vaccine. In this case the **LHRH**-DT molecule induces production of antibodies to GnRH which then serve to inactivate endogenous **LHRH** in the circulation. Without the endogenous **LHRH**, there is no stimulation of the anterior pituitary gland to secrete LH and the gonads will cease functioning. However, as. . .
SUMM . . . medicine as well. For example, the potential for achieving chemical castration (rather than "surgical" castration) with certain luteinizing hormone-releasing hormone (**LHRH**) analogs has been reported (see for example, Javadpour, N., Luteinizing Hormone-Releasing Hormone (**LHRH**) in Disseminated Prostatic Cancer; 1M, Vol. 9, No. 11, November 1988). Table I below gives the structure of **LHRH** and the structure of certain analogs (e.g., Goserelin, Leuprolide, **Buserelin** and Nafarelin) of **LHRH** which are capable of temporarily suppressing luteinizing hormone secretion and
thereby suppressing the gonads. As a consequence, these **LHRH** analogs have come to be regarded as a promising new class of agents for the treatment of various host-dependent diseases, especially prostatic cancer. In referring to Table I, it first should be noted that **LHRH** has a decapeptide structure and that substitution of certain amino acids in the sixth and tenth positions of the **LHRH** produce analogs which render agonists that are up to 100 times more potent than the parent **LHRH** compound (hence these compounds are often referred to as "superagonists"). The structures of **LHRH** and the most commonly known **LHRH** superagonists are listed below.
SUMM
STRUCTURES OF **LHRH** AND SOME SUPERAGONISTS

(Superagonists have substitutions at
positions 6 and 10)
##STR1##
SUPERAGONISTS:

Name	Subs. at 6	Subs. at 10	Terminator
Goserelin:			
	D-Ser(tBu)	AzaGly	Amide
Leuprolide:			
	D-Leu	des-Gly	Ethylamide
Buserelin:			
	D-Ser(tBu)	des-Gly	Ethylamide
Nafarelin:			
	D-2-NaphthylAla		
		None	Amide

SUMM . . . inhibit steroid-dependent tumor growth is through administration of counter-regulatory hormones (e.g., DES in prostate cancer), sex-steroid hormone binding inhibitors (e.g., **tamoxifen** in breast cancer) or surgical castration. Thus the potential medical uses of such chemical castration compounds are vast and varied.. . . appropriately administered sex steroids, desirable antifertility effects can be achieved. Another area of application in human medicine is treatment of **endometriosis**. This condition, which produces painful growth of endometrial tissue in the female peritoneum and pelvis also responds to inhibition of. . .

CLM What is claimed is:
. . . wherein said sex hormone related disease is selected from the group consisting of breast cancer, prostate cancer, pancreatic cancer, and **endometriosis**.

L10 ANSWER 7 OF 24 USPATFULL

AB Methods of treatment and prevention of estrogen-related diseases, and of fertility control, include low dose (e.g. less than 50 nanomolar serum concentration)administration of certain anabolic steroids, progestins and other substantially non-masculinizing androgenic compounds. Sustained release formulations substantially free of organic solvent, and sustained release formulations for maintaining low serum levels of androgen are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	97:40782 USPATFULL		
TITLE:	Controlled release systems and low dose androgens		
INVENTOR(S):	Labrie, Fernand, Quebec, Canada Lepage, Martin, Quebec, Canada		
PATENT ASSIGNEE(S):	Endorecherche Inc., Quebec, Canada (non-U.S. corporation)		
	NUMBER	DATE	
PATENT INFORMATION:	US 5629303	19970513	<--
APPLICATION INFO.:	US 95-398096	19950303 (8)	
RELATED APPLN. INFO.:	Division of Ser. No. US 92-900817, filed on 24 Jun 1992, now patented, Pat. No. US 5434146 which is a continuation-in-part of Ser. No. US 91-724532, filed on 28 Jun 1991, now abandoned		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Nutter, Nathan M.		
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen, LLP		
NUMBER OF CLAIMS:	16		

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 2380
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5629303 19970513 <--
SUMM This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating **endometriosis** in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits containing active ingredients. . .
SUMM . . . for breast and endometrial cancer as well as for the prevention and treatment of bone loss and for treatment of **endometriosis**. The main approaches for the treatment of already developed breast cancer are related to the inhibition of estrogen action and/or. . .
SUMM . . . two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists (**LHRH** agonists) which, following inhibition of secretion of bioactive Luteinizing Hormone (LH) by the pituitary gland, decrease serum estrogens to castrated. . .
SUMM Several studies show that treatment of premenopausal breast cancer patients with **LHRH** agonists induces responses comparable to those achieved with other forms of castration (Klijn et al., J. Steroid Biochem. 20: 1381, 1984; Manni et al., Endocr. Rev. 7: 89-94, 1986). Beneficial effects of treatment with **LHRH** agonists have also been observed in postmenopausal women (Nicholson et al., J. Steroid Biochem. 23: 843-848, 1985).
SUMM U.S. Pat. No. 4,071,622 relates to the use of certain **LHRH** agonists against DMBA-induced mammary carcinoma in rats.
SUMM . . . No. 4,760,053 describes a treatment of selected sex steroid dependent cancers which includes various specified combinations of compounds selected from **LHRH** agonists, antiandrogens, antiestrogens and certain inhibitors of sex steroid biosynthesis.
SUMM . . . 4,472,382 relates to treatment of prostatic adenocarcinoma, benign prostatic hypertrophy and hormone-dependent mammary tumors with specified pharmaceuticals or combinations. Various **LHRH** agonists and antiandrogens are discussed.
SUMM . . . warm-blooded animals which may include inhibition of ovarian hormonal secretion by surgical means (ovariectomy) or chemical means (use of an **LHRH** agonist, e.g. [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10]**LHRH** ethylamide, or antagonists) as part of a combination therapy. Antiestrogens, androgens, progestins, inhibitors of sex steroid formation (especially of 17.beta.-hydroxysteroid. . .
SUMM . . . months has recently been observed in a group of 33 postmenopausal women who previously failed or did not respond to **Tamoxifen** (Manni et al., Cancer 48: 2507-2509, 1981) upon treatment with Fluoxymesterone (Halostatin) (10 mg, b.i.d.). Of these women, 17 had. . . also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to **Tamoxifen** and in those who had failed. Of the 17 patients who had failed to both **Tamoxifen** and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either **Tamoxifen** or hypophysectomy.
SUMM The combination Fluoxymesterone and **Tamoxifen** has been shown to be superior to **Tamoxifen** alone. In fact, complete responses (CR) were seen only in the combination arm while 32% showed partial response (PR) in. . . Ann. Int. Med. 98: 139-144, 1983). Moreover, the median time from onset of therapy to treatment failure was longer with Fluoxymesterone+**Tamoxifen** (180 days) compared to the **Tamoxifen** arm alone (64 days). There was a tendency for improved

survival in the combination therapy arm (380 versus 330 days).

SUMM . . . effect of an androgen combined with an antiestrogen is suggested by the report that patients who did not respond to **Tamoxifen** could respond to Fluoxymesterone and vice versa. Moreover, patients treated with **Tamoxifen** and crossing over to Fluoxymesterone survived longer that those treated with the reverse regimen (Tormey et al., Ann. Int. Med.. . .

SUMM . . . unselected breast cancer patients (Horwitz, J. Steroid Biochem. 27: 447-457, 1987), an efficacy comparable to that of the non-steroidal antiestrogen **tamoxifen** (Lippman, Semin. Oncol. 10 (Suppl.): 11-19, 1983). Its more general use, however, is for breast cancer relapsing after other endocrine. . .

SUMM . . . et al., Am. J. Obstet. Gynecol. 158: 797-807, 1988). The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet. Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

SUMM High dose MPA as first treatment of breast cancer has shown similar effects as **Tamoxifen** (Van Veelen et al., Cancer 58: 7-13, 1986). High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been. . . Am. J. Obstet. Gynecol. 158: 797-807, 1988). High dose MPA is being used with a success similar to that of **Tamoxifen** for the treatment of endometrial carcinoma (Rendina et al., Europ. J. Obstet. Gynecol. Reprod. Biol. 17: 285-291, 1984).

SUMM The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet, Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

SUMM . . . breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for **endometriosis**, has similar undesirable deleterious effects on bone mass in women.

SUMM . . . object of the present invention to provide a method for prevention and treatment of breast cancer, endometrial cancer, osteoporosis and **endometriosis**, while substantially avoiding undesirable side effects.

SUMM . . . activities induced by estrogens. For example, estrogen-related diseases include but are not limited to breast cancer, endometrial cancer, bone loss, **endometriosis** and osteoporosis.

SUMM The methods described herein are particularly useful for the treatment of human breast or endometrial cancer, osteoporosis or **endometriosis**. It is believed that the methods are also suitable for other purposes which are enhanced by administering androgens or otherwise. . .

SUMM . . . for treating or preventing estrogen sensitive diseases and disorders including but not limited to breast cancer, endometrial cancer, osteoporosis and **endometriosis**. The methods comprise administering to a patient in need of such treatment or prevention, an effective amount of sustained release. . .

DETD . . . not only for their more rational use in the prevention and therapy of breast and endometrial cancers as well as **endometriosis** and bone loss but also to avoid side effects caused by interaction with steroid receptors unnecessary for the desired beneficial. . .

DETD . . . breast and endometrial cancer as well as other diseases responsive to activation of the androgen receptor, e.g. bone loss and **endometriosis**. In this invention, the amount of the androgenic compounds administered is much lower than previously used in art for the. . .

DETD . . . scan, chest X-Ray, skeletal survey, ultrasonography of the liver and liver scan (if needed), CAT scan, MRI and physical examination. **Endometriosis** can be diagnosed following pains or

symptoms associated with menstruations in women while definitive diagnosis can be obtained by laparascopy. . .

DETD . . . prevent other signs and symptoms of menopause. In women, when estrogen formation and/or action has been blocked for treatment of **endometriosis**, leiomyomata, breast cancer, uterine cancer, ovarian cancer or other estrogen-sensitive disease, administration of the androgen can be started at any. . .

DETD . . . for use in the prevention and treatment of breast and endometrial cancer as well as bone loss and treatment of **endometriosis** as discussed above. The kits or packages may also contain instructions on how to use the pharmaceutical compositions in accordance. . .

DETD . . . the above therapy using the described regimen, tumor growth of breast and endometrial cancer as well as bone loss and **endometriosis** can be relieved while minimizing adverse side effects. The use of the described regimen can also prevent appearance of the. . .

L10 ANSWER 8 OF 24 USPATFULL

AB The present invention relates to a purified, easily produced poly-.beta.-1.fwdarw.4-N-acetylglucosamine (p-GlcNAc) polysaccharide species. The p-GlcNAc of the invention is a polymer of high molecular weight whose constituent monosaccharide sugars are attached in a .beta.-1.fwdarw.4 conformation, and which is free of proteins, and substantially free of single amino acids, and other organic and inorganic contaminants. In addition, derivatives and reformulations of p-GlcNAc are described. The present invention further relates to methods for the purification of the p-GlcNAc of the invention from microalgae, preferably diatom, starting sources. Still further, the invention relates to methods for the derivatization and reformulation of the p-GlcNAc. Additionally, the present invention relates to the uses of pure p-GlcNAc, its derivatives, and/or its reformulations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	97:35944 USPATFULL
TITLE:	Methods and compositions for poly-.beta.-1-4-N-acetylglucosamine biological barriers
INVENTOR(S):	Vournakis, John N., Hanover, NH, United States Finkielsztein, Sergio, Chestnut Hill, MA, United States Pariser, Ernest R., Belmont, MA, United States Helton, Mike, Memphis, TN, United States
PATENT ASSIGNEE(S):	Marine Polymer Technologies, Inc., Danvers, MA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5624679	19970429	<--
APPLICATION INFO.:	US 95-470083	19950606 (8)	
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 94-347911, filed on 1 Dec 1994 which is a continuation-in-part of Ser. No. US 93-160569, filed on 1 Dec 1993		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Kight, John		
ASSISTANT EXAMINER:	Fonda, Kathleen Kahler		
LEGAL REPRESENTATIVE:	Pennie & Edmonds		
NUMBER OF CLAIMS:	14		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	74 Drawing Figure(s); 58 Drawing Page(s)		
LINE COUNT:	4072		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5624679 19970429 <--

DETD . . . (ara-C) are contemplated for use in the invention as an

improved treatment for acute nonlymphocytic leukemia. Other synergistic combinations include **tamoxifen** with cisplatin for breast cancer, and prostaglandins with cisplatin for breast and prostate cancer. Additionally, many other synergistic combinations of. . .

DETD . . . prednisolone and dexamethasone), estrogens, (diethylstibesterol, estradiol, esterified estrogens, conjugated estrogen, chlorotiasnene), progestins (medroxyprogesterone acetate, hydroxy progesterone caproate, megestrol acetate), antiestrogens (**tamoxifen**), aromastase inhibitors (aminoglutethimide), androgens (testosterone propionate, methyltestosterone, fluoxymesterone, testolactone), antiandrogens (flutamide), **LHRH** analogues (leuprolide acetate), and endocrines for prostate cancer (ketoconazole).

DETD . . . in trauma wounds, for example, spleen, liver and blood vessel injuries; in standard and minimally invasive surgical procedures, for example, **endometriosis** surgery and operations on the gallbladder; in soft and hard tissue wound repair, for example, skin wounds and burn healing;. . .

L10 ANSWER 9 OF 24 USPATFULL

AB Certain steroidal and non-steroidal compounds have been found to inhibit androgen and estrogen formation. Such inhibition may aid in the reduction of the activity of these hormones and may be useful in the treatment of diseases where, for example, inhibition of androgen or estrogen activity is desired. Preferred inhibitors also possess antiestrogenic activity, thus providing the advantage of a double inhibitory action both on estrogen formation and on estrogen action (blockade of estrogen receptors by antiestrogenic action).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	96:116412 USPATFULL	
TITLE:	Inhibitors of sex steroid biosynthesis and methods for their production and use	
INVENTOR(S):	Labrie, Fernand, Ste.-Foy, Canada Merand, Yves, Ste.-Foy, Canada	
PATENT ASSIGNEE(S):	Endorecherche Inc., Canada (non-U.S. corporation)	
	NUMBER	DATE
PATENT INFORMATION:	US 5585405	19961217 <--
APPLICATION INFO.:	US 94-283989	19940801 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 92-966112, filed on 22 Oct 1992, now patented, Pat. No. US 5364847 which is a continuation of Ser. No. US 89-322154, filed on 10 Mar 1989, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Jordan, Kimberly	
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen, LLP	
NUMBER OF CLAIMS:	7	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	1357	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5585405 19961217 <--

DETD . . . are not limited to, malignant as well as non-malignant steroid-sensitive diseases, especially breast cancer, prostate cancer, ovarian cancer, endometrial cancer, **endometriosis**, uterine leiomyomata, precocious puberty, hirsutism, acne, seborrhea, androgenic alopecia benign prostatic hyperplasia, sexual deviants as well as for male and. . .

DETD In particular, a preferred inhibitor produces antisteroid effects at a dose possessing no agonistic activity, unlike compounds such as **Tamoxifen**, which possesses some agonistic properties which limit their therapeutical efficiency (Wakeling and Bowler, J. Steroid Biochem.

30, 141-147, 1988).
DETD . . . and antiandrogens are beneficial. In particular this approach is of value in breast cancer, prostate cancer, endometrial cancer, ovarian cancer, **endometriosis**, benign prostatic hyperplasia, precocious puberty, hirsutism, acne, seborrhea, androgenic alopecia, menstrual disorders and as male and female contraceptive as well. . .
DETD . . . dosage of the above-described compound (multi sex hormone blocker) are the same as in intact patients or patients receiving an **LHRH** agonist or antagonist.

L10 ANSWER 10 OF 24 USPATFULL
AB A method of treatment or prevention of breast and endometrial cancer, osteoporosis and **endometriosis** in susceptible warm-blooded animals comprising administering a low dose of a progestin or other steroid derivative having androgenic activity and low masculinizing activity. Pharmaceutical compositions useful for such treatment and pharmaceutical kits containing such compositions are disclosed. An in vitro assay permitting specific measurements of androgenic activity of potentially useful compounds is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 96:97032 USPATFULL
TITLE: Methods for preventing and treating osteoporosis with low dose non-masculinizing androgenic compounds
INVENTOR(S): Labrie, Fernand, Quebec, Canada
PATENT ASSIGNEE(S): Endorecherche, Inc., Quebec, Canada (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5567695	19961022	<--
APPLICATION INFO.:	US 95-483761	19950607 (8)	

RELATED APPLN. INFO.: Division of Ser. No. US 94-282964, filed on 29 Jul 1994
which is a division of Ser. No. US 93-15083, filed on 8 Feb 1993, now patented, Pat. No. US 5362720 which is a continuation of Ser. No. US 91-724532, filed on 28 Jun 1991, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Nutter, Nathan M.
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen, LLP
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1453
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5567695 19961022 <--
AB A method of treatment or prevention of breast and endometrial cancer, osteoporosis and **endometriosis** in susceptible warm-blooded animals comprising administering a low dose of a progestin or other steroid derivative having androgenic activity and. . .
SUMM This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating **endometriosis** in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits containing active ingredients. . .
SUMM . . . for breast and endometrial cancer as well as for the prevention and treatment of bone loss and for treatment of **endometriosis**. The main approaches for the treatment of already developed breast cancer are related to the inhibition of estrogen action and/or. . .
SUMM . . . two procedures giving irreversible castration. Recently, a

reversible form of castration has been achieved by utilizing Luteinizing
Hormone-Releasing Hormone Agonists (**LHRH** agonists) which, following inhibition of secretion of bioactive Luteinizing Hormone (LH) by the pituitary gland, decrease serum estrogens to castrated. . .

SUMM Several studies show that treatment of premenopausal breast cancer patients with **LHRH** agonists induces responses comparable to those achieved with other forms of castration (Klijn et al., J. Steroid Biochem. 20:1381, 1984; Manni et al., Endocr. Rev. 7:89-94, 1986). Beneficial effects of treatment with **LHRH** agonists have also been observed in postmenopausal women (Nicholson et al., J. Steroid Biochem. 23:843-848, 1985).

SUMM U.S. Pat. No. 4,071,622 relates to the use of certain **LHRH** agonists against DMBA-induced mammary carcinoma in rats.

SUMM . . . No. 4,760,053 describes a treatment of selected sex steroid dependent cancers which includes various specified combinations of compounds selected from **LHRH** agonists, antiandrogens, antiestrogens and certain inhibitors of sex steroid biosynthesis.

SUMM . . . 4,472,382 relates to treatment of prostatic adenocarcinoma, benign prostatic hypertrophy and hormone-dependent mammary tumors with specified pharmaceuticals or combinations. Various **LHRH** agonists and antiandrogens are discussed.

SUMM . . . warm-blooded animals which may include inhibition of ovarian hormonal secretion by surgical means (ovariectomy) or chemical means (use of an **LHRH** agonist, e.g. [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10]**LHRH** ethylamide, or antagonists) as part of a combination therapy. Antiestrogens, androgens, progestins, inhibitors of sex steroid formation (especially of 17.beta.-hydroxysteroid. . .

SUMM . . . months has recently been observed in a group of 33 postmenopausal women who previously failed or did not respond to **Tamoxifen** (Manni et al., Cancer 48:2507-2509, 1981) upon treatment with Fluoxymesterone (Halostatin) (10 mg, b.i.d.). Of these women, 17 had also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to **Tamoxifen** and in those who had failed. Of the 17 patients who had failed to both **Tamoxifen** and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either **Tamoxifen** or hypophysectomy.

SUMM The combination Fluoxymesterone and **Tamoxifen** has been shown to be superior to **Tamoxifen** alone. In fact, complete responses (CR) were seen only in the combination arm while 32% showed partial response (PR) in. . . al., Ann. Int. Med. 98:139-144, 1983). Moreover, the median time from onset of therapy to treatment failure was
longer with Fluoxymesterone+**Tamoxifen** (180 days) compared to the **Tamoxifen** arm alone (64 days). There was a tendency for improved survival in the combination therapy arm (380 versus 330 days).

SUMM . . . effect of an androgen combined with an antiestrogen is suggested by the report that patients who did not respond to **Tamoxifen** could respond to Fluoxymesterone and vice versa. Moreover, patients treated with **Tamoxifen** and crossing over to Fluoxymesterone survived longer that those treated with the reverse regimen (Tormey et al., Ann. Int. Med.. . .

SUMM . . . in unselected breast cancer patients (Horwitz, J. Steroid Biochem. 27:447-457, 1987), an efficacy comparable to that of the non-steroidal antiestrogen **tamoxifen** (Lippman, Semin. Oncol. 10 (Suppl.): 11-19, 1983). Its more general use, however, is for breast cancer relapsing after other endocrine. . .

SUMM High dose MPA as first treatment of breast cancer has shown similar effects as **Tamoxifen** (Van Veelen et al., Cancer 58:7-13, 1986). High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been successfully. . . al., Am. J. Obstet. Gynecol. 158:797-807, 1988). High dose MPA is being used with a success similar to that of **Tamoxifen** for the treatment of

endometrial carcinoma (Rendina et al., Europ. J. Obstet. Gynecol. Reprod. Biol. 17:285-291, 1984).

SUMM The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50:743, 1987; Preston, Obstet, Gynecol. 2:152, 1965). Androgenic and masculinizing side effects (sometimes irreversible) are however. . .

SUMM . . . breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for **endometriosis**, has similar undesirable deleterious effects on bone mass in women.

SUMM . . . object of the present invention to provide a method for prevention and treatment of breast cancer, endometrial cancer, osteoporosis and **endometriosis**, while substantially avoiding undesirable side effects.

SUMM . . . of said androgenic steroid described herein are particularly useful for the treatment of human breast or endometrial cancer, osteoporosis or **endometriosis**. It is believed that the methods are also suitable for all purposes which are enhanced by administering androgens or otherwise. . .

DETD . . . not only for their more rational use in the prevention and therapy of breast and endometrial cancers as well as **endometriois** and bone loss but also to avoid side effects caused by interaction with steroid receptors unnecessary for the desired beneficial. . .

DETD . . . breast and endometrial cancer as well as other diseases responsive to activation of the androgen receptor, e.g. bone loss and **endometriosis**. In this invention, the amount of the androgenic compounds administered is much lower than previously used in art for the. . .

DETD . . . scan, chest X-Ray, skeletal survey, ultrasonography of the liver and liver scan (if needed), CAT scan, MRI and physical examination. **Endometriosis** can be diagnosed following pains or symptoms assodated with menstruations in women while definitive diagnosis can be obtained by laparascopy. . .

DETD . . . prevent other signs and symptoms of menopause. In women, when estrogen formation and/or action has been blocked for treatment of **endometriosis**, leiomyomata, breast cancer, uterine cancer, ovarian cancer or other estrogen-sensitive disease, administration of the androgen can be started at any. . .

DETD . . . for use in the prevention and treatment of breast and endometrial cancer as well as bone loss and treatment of **endometriosis** as discussed above. The kits or packages may also contain instructions on how to use the pharmaceutical compositions in accordance. . .

DETD . . . the above therapy using the described regimen, tumor growth of breast and endometrial cancer as well as bone loss and **endometriosis** can be relieved while minimizing adverse side effects. The use of the described regimen can also prevent appearance of the. . .

L10 ANSWER 11 OF 24 USPATFULL

AB A method of treatment or prevention of breast and endometrial cancer, osteoporosis and **endometriosis** in susceptible warm-blooded animals comprising administering a low dose. Of a progestin or other steroid derivative having androgenic activity and low masculinizing activity. Pharmaceutical compositions useful for such treatment and pharmaceutical kits containing such compositions are disclosed. An in vitro assay permitting specific measurements of androgenic activity of potentially useful compounds is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 96:72882 USPATFULL

TITLE: Activation of androgen receptors with low dose non-masculinizing androgenic compounds

INVENTOR(S): Labrie, Fernand, Quebec, Canada
PATENT ASSIGNEE(S): Endorecherche, Inc., Quebec, Canada (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5545634	19960813	<--
APPLICATION INFO.:	US 94-282964	19940729 (8)	

RELATED APPLN. INFO.: Division of Ser. No. US 93-15083, filed on 8 Feb 1993, now patented, Pat. No. US 5362720 which is a continuation of Ser. No. US 91-724532, filed on 28 Jun 1991, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Nutter, Nathan M.
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen, LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1406
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5545634 19960813 <--

AB A method of treatment or prevention of breast and endometrial cancer, osteoporosis and **endometriosis** in susceptible warm-blooded animals comprising administering a low dose. Of a progestin or other steroid derivative having androgenic activity and. . .

SUMM This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating **endometriosis** in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits containing active ingredients. . .

SUMM . . . for breast and endometrial cancer as well as for the prevention and treatment of bone loss and for treatment of **endometriosis**. The main approaches for the treatment of already developed breast cancer are related to the inhibition of estrogen action and/or. . .

SUMM . . . two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists (**LHRH** agonists) which, following inhibition of secretion of bioactive Luteinizing Hormone (LH) by the pituitary gland, decrease serum estrogens to castrated. . .

SUMM Several studies show that treatment of premenopausal breast cancer patients with **LHRH** agonists induces responses comparable to those achieved with other forms of castration (Klijn et al., J. Steroid Biochem. 20: 1381, 1984; Manni et al., Endocr. Rev. 7: 89,-94, 1986). Beneficial effects of treatment with **LHRH** agonists have also been observed in postmenopausal women (Nicholson et al., J. Steroid Biochem. 23: 843-848, 1985).

SUMM U.S. Pat. No. 4,071,622 relates to the use of certain **LHRH** agonists against DMBA-induced mammary carcinoma in rats.

SUMM . . . No. 4,760,053 describes a treatment of selected sex steroid dependent cancers which includes various specified combinations of compounds selected from **LHRH** agonists, antiandrogens, antiestrogens and certain inhibitors of sex steroid biosynthesis.

SUMM . . . 4,472,382 relates to treatment of prostatic adenocarcinoma, benign prostatic hypertrophy and hormone-dependent mammary tumors with specified pharmaceuticals or combinations. Various **LHRH** agonists and antiandrogens are discussed.

SUMM . . . warm-blooded animals which may include inhibition of ovarian hormonal secretion by surgical means (ovariectomy) or chemical means (use of an **LHRH** agonist, e.g. [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10]**LHRH** ethylamide, or antagonists) as part of a combination therapy. Antiestrogens, androgens, progestins,

inhibitors of sex steroid formation (especially of 17.beta.-hydroxysteroid. . .

SUMM . . . months has recently been observed in a group of 33 postmenopausal women who previously failed or did not respond to **Tamoxifen** (Manni et al., Cancer 48: 2507-2509, 1981) upon treatment with Fluoxymesterone (Halostatin) (10 mg, b.i.d.). Of these women, 17 had. . . also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to **Tamoxifen** and in those who had failed. Of the 17 patients who had failed to both **Tamoxifen** and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either **Tamoxifen** or hypophysectomy.

SUMM The combination Fluoxymesterone and **Tamoxifen** has been shown to be superior to **Tamoxifen** alone. In fact, complete responses (CR) were seen only in the combination arm while 32% showed partial response (PR) in. . . Ann. Int. Med. 98: 139-144, 1983). Moreover, the median time from onset of therapy to treatment failure was longer with Fluoxymesterone+**Tamoxifen** (180 days) compared to the **Tamoxifen** arm alone (64 days). There was a tendency for improved survival in the combination therapy arm (380 versus 330 days).

SUMM . . . effect of an androgen combined with an antiestrogen is suggested by the report that patients who did not respond to **Tamoxifen** could respond to Fluoxymesterone and vice versa. Moreover, patients treated with **Tamoxifen** and crossing over to Fluoxymesterone survived longer that those treated with the reverse regimen (Tormey et al., Ann. Int. Med.. . .

SUMM . . . unselected breast cancer patients (Horwitz, J. Steroid Biochem. 27: 447-457, 1987), an efficacy comparable to that of the non-steroidal antiestrogen **tamoxifen** (Lippman, Semin. Oncol. 10 (Suppl.): 11-19, 1983). Its more general use, however, is for breast cancer relapsing after other endocrine. . .

SUMM High dose MPA as first treatment of breast cancer has shown similar effects as **Tamoxifen** (Van Veelen et al., Cancer 58: 7-13, 1986). High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been. . . Am. J. Obstet. Gynecol. 158: 797-807, 1988). High dose MPA is being used with a success similar to that of **Tamoxifen** for the treatment of endometrial carcinoma (Rendina et al., Europ. J. Obstet. Gynecol. Reprod. Biol. 17: 285-291, 1984). In a. . .

SUMM The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet, Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

SUMM . . . breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for **endometriosis**, has similar undesirable deleterious effects on bone mass in women.

SUMM . . . object of the present invention to provide a method for prevention and treatment of breast cancer, endometrial cancer, osteoporosis and **endometriosis**, while substantially avoiding undesirable side effects.

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DETD . . . not only for their more rational use in the prevention and therapy of breast and endometrial cancers as well as **endometriois** and bone loss but also to avoid side effects caused by interaction with steroid receptors unnecessary for the desired beneficial. . .

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DETD . . . scan, chest X-Ray, skeletal survey, ultrasonography of the liver and liver scan (if needed), CAT scan, MRI and physical examination. **Endometriosis** can be diagnosed following pains or symptoms associated with menstruations in women while definitive diagnosis can be obtained by laparascopy. . .

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DETD . . . the above therapy using the described regimen, tumor growth of breast and endometrial cancer as well as bone loss and **endometriosis** can be relieved while minimizing adverse side effects. The use of the described regimen can also prevent appearance of the. . .

L10 ANSWER 12 OF 24 USPATFULL

AB Methods of treatment and prevention of estrogen-related diseases, and of fertility control, include low dose (e.g. less than 50 nanomolar serum concentration) administration of certain anabolic steroids, progestins and other substantially non-masculinizing androgenic compounds. Sustained release formulations substantially free of organic solvent, and sustained release formulations for maintaining low serum levels of androgen are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	96:67992 USPATFULL	
TITLE:	Controlled release systems and low dose androgens	
INVENTOR(S):	Labrie, Fernand, Quebec, Canada Lepage, Martin, Quebec, Canada	
PATENT ASSIGNEE(S):	Endorecherche, Inc., Canada (non-U.S. corporation)	
	NUMBER	DATE
PATENT INFORMATION:	US 5541172	19960730 <--
APPLICATION INFO.:	US 95-474347	19950607 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 95-398096, filed on 3 Mar 1995 which is a division of Ser. No. US 92-900817, filed on 24 Jun 1992 which is a continuation-in-part of Ser. No. US 91-724532, filed on 28 Jun 1991	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Nutter, Nathan M.	
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen	
NUMBER OF CLAIMS:	1	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	17 Drawing Figure(s); 13 Drawing Page(s)	
LINE COUNT:	2236	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5541172 19960730 <--

SUMM This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating **endometriosis** in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits

containing active ingredients. . .

SUMM . . . for breast and endometrial cancer as well as for the prevention and treatment of bone loss and for treatment of **endometriosis**. The main approaches for the treatment of already developed breast cancer are related to the inhibition of estrogen action and/or. . .

SUMM . . . two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists (**LHRH** agonists) which, following inhibition of secretion of bioactive Luteinizing Hormone (LH) by the pituitary gland, decrease serum estrogens to castrated. . .

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SUMM . . . et al., Am. J. Obstet. Gynecol. 158: 797-807, 1988). The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet. Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

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SUMM . . . breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for **endometriosis**, has similar undesirable deleterious effects on bone mass in women.

SUMM . . . object of the present invention to provide a method for prevention and treatment of breast cancer, endometrial cancer, osteoporosis and **endometriosis**, while substantially avoiding undesirable side effects.

SUMM . . . activities induced by estrogens. For example, estrogen-related diseases include but are not limited to breast cancer, endometrial cancer, bone loss, **endometriosis** and osteoporosis.

SUMM The methods described herein are particularly useful for the treatment of human breast or endometrial cancer, osteoporosis or **endometriosis**. It is believed that the methods are also suitable for other purposes which are enhanced by administering androgens or otherwise. . .

SUMM . . . for treating or preventing estrogen sensitive diseases and disorders including but not limited to breast cancer, endometrial cancer, osteoporosis and **endometriosis**. The methods comprise administering to a patient in need of such treatment or prevention, an effective amount of sustained release. . .

DETD . . . not only for their more rational use in the prevention and therapy of breast and endometrial cancers as well as **endometriosis** and bone loss but also to avoid side effects caused by interaction with steroid receptors unnecessary for the desired beneficial. . .

DETD . . . breast and endometrial cancer as well as other diseases responsive to activation of the androgen receptor, e.g. bone loss and **endometriosis**. In this invention, the amount of the androgenic compounds administered is much lower than previously used in art for the. . .

DETD . . . scan, chest X-Ray, skeletal survey, ultrasonography of the liver and liver scan (if needed), CAT scan, MRI and physical examination. **Endometriosis** can be diagnosed following pains or symptoms associated with menstruations in women while definitive diagnosis can be obtained by laparascopy. . .

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DETD . . . the above therapy using the described regimen, tumor growth of

breast and endometrial cancer as well as bone loss and **endometriosis** can be relieved while minimizing adverse side effects. The use of the described regimen can also prevent appearance of the. . .

L10 ANSWER 13 OF 24 USPATFULL

AB Certain toxic compounds (T) such as, for example, compounds based upon diphtheria toxin, ricin toxin, pseudomonas exotoxin, .alpha.-amanitin, pokeweed antiviral protein (PAP), ribosome inhibiting proteins, especially the ribosome inhibiting proteins of barley, wheat, corn, rye, gelonin and abrin, as well as certain cytotoxic chemicals such as, for example, melphalan and daunomycin can be conjugated to certain analogs of gonadotropin-releasing hormone to form a class of compounds which, when injected into an animal, destroy the gonadotrophs of the animal's anterior pituitary gland. Hence such compounds may be used to sterilize such animals and/or to treat certain sex hormone related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	96:14794 USPATFULL	
TITLE:	Hormone-toxin conjugate compounds	
INVENTOR(S):	Nett, Torrance M., Ft. Collins, CO, United States Glode, Leonard M., Aurora, CO, United States	
PATENT ASSIGNEE(S):	Colorado State University Research Foundation, Fort Collins, CO, United States (U.S. corporation)	
	NUMBER	DATE
PATENT INFORMATION:	US 5492893	19960220 <--
APPLICATION INFO.:	US 93-94250	19930720 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 92-837639, filed on 14 Feb 1992, now patented, Pat. No. US 5378688 which is a continuation-in-part of Ser. No. US 89-314653, filed on 23 Feb 1989, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Warden, Jill	
ASSISTANT EXAMINER:	Huff, Sheela J.	
LEGAL REPRESENTATIVE:	Sheridan Ross & McIntosh	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)	
LINE COUNT:	1435	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5492893 19960220 <--

SUMM . . . of the steroidal hormones, estradiol, progesterone and testosterone. It should also be noted that the terms "GnRH" (gonadotropin-releasing hormone) and "**LHRH**" (luteinizing hormone-releasing hormone) are sometimes used interchangeably in the literature. For the purposes of describing the prior art both terms. .

SUMM . . . this regard was recently published in the INTERNATIONAL JOURNAL OF PHARMACOLOGY 76:R5-R8 by Singh et al. entitled "Controlled release of **LHRH**-DT from bioerodible hydrogel microspheres." Generally speaking, it teaches that a natural GnRH/diphtheria toxin can be used as a vaccine. In this case the **LHRH**-DT molecule induces production of antibodies to GnRH which then serve to inactivate endogenous **LHRH** in the circulation. Without the endogenous **LHRH**, there is no stimulation of the anterior pituitary gland to secrete LH and the gonads will cease functioning. However, as. . .

SUMM . . . medicine as well. For example, the potential for achieving chemical castration (rather than "surgical" castration) with certain

luteinizing hormone-releasing hormone (**LHRH**) analogs has been reported (see for example, Javadpour, N., Luteinizing Hormone-Releasing Hormone (**LHRH**) in Disseminated Prostatic Cancer; 1M, Vol. 9, No. 11, November 1988). Table I below gives the structure of **LHRH** and the structure of certain analogs (e.g., Goserelin, Leuprolide, **Buserelin** and Nafarelin) of **LHRH** which are capable of temporarily suppressing luteinizing hormone secretion and thereby suppressing the gonads. As a consequence, these **LHRH** analogs have come to be regarded as a promising new class of agents for the treatment of various host-dependent diseases, especially prostatic cancer. In referring to Table I, it first should be noted that **LHRH** has a decapeptide structure and that substitution of certain amino acids in the sixth and tenth positions of the **LHRH** produce analogs which render agonists that are up to 100 times more potent than the parent **LHRH** compound (hence these compounds are often referred to as "superagonists"). The structures of **LHRH** and the most commonly known **LHRH** superagonists are listed below.

SUMM

STRUCTURES OF **LHRH** AND SOME SUPERAGONISTS
(Superagonists have substitutions at positions 6 and 10)

LHRH:

pGlu--His--Trp--Ser--Tyr--Gly--Leu--Arg--Pro--Gly--NH.sub.2
1 2 3 4 5 6 7 8 9 10

SUPERAGONISTS:

Name	Subs. at 6	Subs. at 10	Terminator
Goserelin:	D-Ser(tBu)	AzaGly	Amide
Leuprolide:	D-Leu	des-Gly	Ethylamide
Buserelin:	D-Ser(tBu)	des-Gly	Ethylamide
Nafarelin:	D-2-NaphthylAla	None	Amide

SUMM . . . inhibit steroid-dependent tumor growth is through administration of counter-regulatory hormones (e.g., DES in prostate cancer), sex-steroid hormone binding inhibitors (e.g., **tamoxifen** in breast cancer) or surgical castration. Thus the potential medical uses of such chemical castration compounds are vast and varied.. . . appropriately administered sex steroids, desirable antifertility effects can be achieved. Another area of application in human medicine is treatment of **endometriosis**. This condition, which produces painful growth of endometrial tissue in the female peritoneum and pelvis also responds to inhibition of. . .

L10 ANSWER 14 OF 24 USPATFULL

AB Certain toxic compounds (T) such as, for example, compounds based upon diphtheria toxin, ricin toxin, pseudomonas exotoxin, .alpha.-amanitin, pokeweed antiviral protein (PAP), ribosome inhibiting proteins, especially the ribosome inhibiting proteins of barley, wheat, corn, rye, gelonin and abrin, as well as certain cytotoxic chemicals such as, for example, melphalan and daunomycin can be conjugated to certain analogs of gonadotropin-releasing hormone to form a class of compounds which, when injected into an animal, destroy the gonadotrophs of the animal's anterior pituitary gland. Hence such compounds may be used to sterilize such animals and/or to treat certain sex hormone related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 96:9411 USPATFULL
TITLE: Method for sterilizing animals using hormone-toxin conjugate compounds
INVENTOR(S): Nett, Torrance M., Ft. Collins, CO, United States
Glode, Leonard M., Aurora, CO, United States
PATENT ASSIGNEE(S): Colorado State University Research Foundation, Fort Collins, CO, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5488036	19960130	<--
APPLICATION INFO.:	US 93-94625	19930720 (8)	

RELATED APPLN. INFO.: Division of Ser. No. US 92-837639, filed on 14 Feb 1992, now patented, Pat. No. US 5378688 which is a continuation-in-part of Ser. No. US 89-314653, filed on
23 Feb 1989, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Warden, Jill
ASSISTANT EXAMINER: Huff, Sheila J.
LEGAL REPRESENTATIVE: Sheridan Ross & McIntosh
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1447
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5488036 19960130 <--
SUMM . . . of the steroidal hormones, estradiol, progesterone and testosterone. It should also be noted that the terms "GnRH" (gonadotropin-releasing hormone) and "**LHRH**" (luteinizing hormone-releasing hormone) are sometimes used interchangeably in the literature. For the purposes of describing the prior art both terms. . .
SUMM . . . regard was recently published in the INTERNATIONAL JOURNAL OF PHARMACOLOGY 76: R5-R8 by Singh et al. entitled "Controlled release of **LHRH**-DT from bioerodible hydrogel microspheres." Generally speaking, it teaches that a natural GnRH/diphtheria toxin can be used as a vaccine. In this case the **LHRH**-DT molecule induces production of antibodies to GnRH which then serve to inactivate endogenous **LHRH** in the circulation. Without the endogenous **LHRH**, there is no stimulation of the anterior pituitary gland to secrete LH and the gonads will cease functioning. However, as. . .
SUMM . . . medicine as well. For example, the potential for achieving chemical castration (rather than "surgical" castration) with certain luteinizing hormone-releasing hormone (**LHRH**) analogs has been reported (see for example, Javadpour, N., Luteinizing Hormone-Releasing Hormone (**LHRH**) in Disseminated Prostatic Cancer; 1M, Vol. 9, No. 11, November 1988). Table I below gives the structure of **LHRH** and the structure of certain analogs (e.g., Goserelin, Leuprolide, **Buserelin** and Nafarelin) of **LHRH** which are capable of temporarily suppressing luteinizing hormone secretion and thereby suppressing the gonads. As a consequence, these **LHRH** analogs have come to be regarded as a promising new class of agents for the treatment of various host-dependent diseases, especially prostatic cancer. In referring to Table I, it first should be noted that **LHRH** has a decapeptide structure and that substitution of certain amino acids in the sixth and tenth positions of the **LHRH** produce analogs which render agonists that are up to 100 times more potent than the parent **LHRH** compound (hence these compounds are often referred to as "superagonists"). The structures of **LHRH** and the most commonly known **LHRH** superagonists are listed below.
SUMM STRUCTURES OF **LHRH** AND SOME SUPERAGONISTS

SUMM

LHRH:

pGlu--His--Trp--Ser--Tyr--Gly--Leu--Arg--Pro--Gly--NH.sub.2

1 2 3 4 5 6 7 8 9 10

SUPERAGONISTS:

Name	Subs. at 6	Subs. at 10	Terminator
Goserelin:			
	D-Ser(tBu)	AzaGly	Amide
Leuprolide:			
	D-Leu	des-Gly	Ethylamide
Buserelin:			
	D-Ser(tBu)	des-Gly	Ethylamide
Nafarelin:			
	D-2-NaphthylAla		
		None	Amide

SUMM . . . inhibit steroid-dependent tumor growth is through administration of counter-regulatory hormones (e.g., DES in prostate cancer), sex-steroid hormone binding inhibitors (e.g., **tamoxifen** in breast cancer) or surgical castration. Thus the potential medical uses of such chemical castration compounds are vast and varied.. . . appropriately administered sex steroids, desirable antifertility effects can be achieved. Another area of application in human medicine is treatment of **endometriosis**. This condition, which produces painful growth of endometrial tissue in the female peritoneum and pelvis also responds to inhibition of. . .

CLM What is claimed is:

. . . said sex hormone related disease selected from the group consisting of breast cancer, prostate cancer, sex-steroid dependent tumors, osteoporosis and **endometriosis**, said conjugate by a linking agent comprising a peptide hormone capable of binding to a GnRH receptor, conjugated to a. . .

L10 ANSWER 15 OF 24 USPATFULL

AB Methods of treatment and prevention of estrogen-related diseases, and of fertility control, include low dose (e.g. less than 50 nanomolaR serum concentration) administration of certain anabolic steroids, progestins and other substantially non-masculinizing androgenic compounds. Sustained release formulations substantially free of organic solvent, and sustained release formulations for maintaining low serum levels of androgen are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	95:64916 USPATFULL		
TITLE:	Controlled release systems and low dose androgens		
INVENTOR(S):	Labrie, Fernand, Quebec, Canada Lepage, Martin, Quebec, Canada		
PATENT ASSIGNEE(S):	Endorecherche, Inc., Quebec, Canada (non-U.S. corporation)		
	NUMBER	DATE	
PATENT INFORMATION:	US 5434146	19950718	<--
APPLICATION INFO.:	US 92-900817	19920624 (7)	
DISCLAIMER DATE:	20111108		
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 91-724532, filed on 28 Jun 1991, now abandoned		
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Nutter, Nathan M.		
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen		

NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 2424
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5434146 19950718 <--
SUMM This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating **endometriosis** in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits containing active ingredients. . .
SUMM . . . for breast and endometrial cancer as well as for the prevention and treatment of bone loss and for treatment of **endometriosis**. The main approaches for the treatment of already breast cancer are related to the inhibition of estrogen action and/or formation.. . .
SUMM . . . two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists (**LHRH** agonists) which, following inhibition of secretion of bioactive Luteinizing Hormone (LH) by the pituitary gland, decrease serum estrogens to castrated. . .
SUMM Several studies show that treatment of premenopausal breast cancer patients with **LHRH** agonists induces responses comparable to those achieved with other forms of castration (Klijn et al., J. Steroid Biochem. 20: 1381, 1984; Manni et al., Endocr. Rev. 7: 89-94, 1986). Beneficial effects of treatment with **LHRH** agonists have also been observed in postmenopausal women (Nicholson et al., J. Steroid Biochem. 23: 843-848, 1985).
SUMM U.S. Pat. No. 4,071,622 relates to the use of certain **LHRH** agonists against DMBA-induced mammary carcinoma in rats.
SUMM . . . No. 4,760,053 describes a treatment of selected sex steroid dependent cancers which includes various specified combinations of compounds selected from **LHRH** agonists, antiandrogens, antiestrogens and certain inhibitors of sex steroid biosynthesis.
SUMM . . . 4,472,382 relates to treatment of prostatic adenocarcinoma, benign prostatic hypertrophy and hormone-dependent mammary tumors with specified pharmaceuticals or combinations. Various **LHRH** agonists and antiandrogens are discussed.
SUMM . . . warm-blooded animals which may include inhibition of ovarian hormonal secretion by surgical means (ovariectomy) or chemical means (use of an **LHRH** agonist, e.g. [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10]**LHRH** ethylamide, or antagonists) as part of a combination therapy. Antiestrogens, androgens, progestins, inhibitors of sex steroid formation (especially of 17.beta.-hydroxysteroid. . .
SUMM . . . months has recently been observed in a group of 33 postmenopausal women who previously failed or did not respond to **Tamoxifen** (Manni et al., Cancer 48: 2507-2509, 1981) upon treatment with Fluoxymesterone (Halostatin) (10 mg, b.i.d.). Of these women, 17 had. . . also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to **Tamoxifen** and in those who had failed. Of the 17 patients who had failed to both **Tamoxifen** and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either **Tamoxifen** or hypophysectomy.
SUMM The combination Fluoxymesterone and **Tamoxifen** has been shown to be superior to **Tamoxifen** alone. In fact, complete responses (CR) were seen only in the combination arm while 32% showed partial response (PR) in. . . Ann. Int. Med. 98: 139-144, 1983). Moreover, the median time from onset of therapy to treatment failure was longer with Fluoxymesterone+**Tamoxifen** (180 days) compared to the **Tamoxifen** arm alone (64 days). There was a tendency for improved

survival in the combination therapy arm (380 versus 330 days).

SUMM . . . effect of an androgen combined with an antiestrogen is suggested by the report that patients who did not respond to **Tamoxifen** could respond to Fluoxymesterone and vice versa. Moreover, patients treated with **Tamoxifen** and crossing over to Fluoxymesterone survived longer that those treated with the reverse regimen (Torney et al., Ann. Int. Med.. . .

SUMM . . . unselected breast cancer patients (Horwitz, J. Steroid Biochem. 27: 447-457, 1987), an efficacy comparable to that of the non-steroidal antiestrogen **tamoxifen** (Lippman, Semin. Oncol. 10 (Suppl.): 11-19, 1983). Its more general use, however, is for breast cancer relapsing after other endocrine. . .

SUMM . . . et al., Am. J. Obstet. Gynecol, 158: 797-807, 1988). The androgen methyltesiosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet. Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

SUMM High dose MPA as first treatment of breast cancer has shown similar effects as **Tamoxifen** (Van Veelen et al., Cancer 58: 7-13, 1986). High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been. . . Am. J. Obstet. Gynecol. 158: 797-807, 1988). High dose MPA is being used with a success similar to that of **Tamoxifen** for the treatment of endometrial carcinoma (Rendina et al., Europ. J. Obstet. Gynecol. Reprod. Biol. 17: 285-291, 1984).

SUMM The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet. Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

SUMM . . . breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for **endometriosis**, has similar undesirble deleterious effects on bone mass in women.

SUMM . . . object of the present invention to provide a method for prevention and treatment of breast cancer, endometrial cancer, osteoporosis and **endometriosis**, while substantially avoiding undesirable side effects.

SUMM . . . activities induced by estrogens. For example, estrogen-related diseases include but are not limited to breast cancer, endometrial cancer, bone loss, **endometriosis** and osteoporosis.

SUMM The methods described herein are particularly useful for the treatment of human breast or endometrial cancer, osteoporosis or **endometriosis**. It is believed that the methods are also suitable for other purposes which are enhanced by administering androgens or otherwise. . .

SUMM . . . for treating or preventing estrogen sensitive diseases and disorders including but not limited to breast cancer, endometrial cancer, osteoporosis and **endometriosis**. The methods comprise administering to a patient in need of such treatment or prevention, an effective amount of sustained release. . .

DETD . . . not only for their more rational use in the prevention and therapy of breast and endometrial cancers as well as **endometriosis** and bone loss but also to avoid side effects caused by interaction with steroid receptors unnecessary for the desired beneficial. . .

DETD . . . breast and endometrial cancer as well as other diseases responsive to activation of the androgen receptor, e.g. bone loss and **endometriosis**. In this invention, the amount of the androgenic compounds administered is much lower than previously used in art for the. . .

DETD . . . scan, chest X-Ray, skeletal survey, ultrasonography of the liver and liver scan (if needed), CAT scan, MRI and physical examination. **Endometriosis** can be diagnosed following pains or

symptoms associated with menstruations in women while definitive diagnosis can be obtained by laparascopy. . .

DETD . . . prevent other signs and symptoms of menopause. In women, when estrogen formation and/or action has been blocked for treatment of **endometriosis**, leiomyomata, breast cancer, uterine cancer, ovarian cancer or other estrogen-sensitive disease, administration of the androgen can be started at any. . .

DETD . . . for use in the prevention and treatment of breast and endometrial cancer as well as bone loss and treatment of **endometriosis** as discussed above. The kits or packages may also contain instructions on how to use the pharmaceutical compositions in accordance. . .

DETD . . . the above therapy using the described regimen, tumor growth of breast and endometrial cancer as well as bone loss and **endometriosis** can be relieved while minimizing adverse side effects. The use of the described regimen can also prevent appearance of the. . .

L10 ANSWER 16 OF 24 USPATFULL

AB Inhibitors of sex steroid activity, for example those having the general structure ##STR1## may be used as part of a pharmaceutical composition to provide antiestrogenic effects and/or to suppress estrogen synthesis. Such pharmaceutical compositions are useful for the treatment of breast cancer or other diseases whose progress is aided by activation of sex steroid receptors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	95:20734 USPATFULL	
TITLE:	Anti-estrogenic compounds and compositions	
INVENTOR(S):	Labrie, Fernand, Quebec, Canada Merand, Yves, Quebec, Canada	
PATENT ASSIGNEE(S):	Endorecherche Inc., Canada (non-U.S. corporation)	
	NUMBER	DATE
PATENT INFORMATION:	US 5395842	19950307 <--
APPLICATION INFO.:	US 91-801704	19911202 (7)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 88-265150, filed on 31 Oct 1988, now abandoned And a continuation-in-part of Ser. No. US 89-377010, filed on 7 Jul 1989, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Cintins, Marianne M.	
ASSISTANT EXAMINER:	Criares, T. J.	
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen	
NUMBER OF CLAIMS:	66	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	3525	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5395842 19950307 <--

SUMM H. Mouridsen et al., Cancer Treatm. Rev. 5: 131-141 (1978), discloses that **Tamoxifen**, an antiestrogen, is effective in remission of advanced breast cancer in about 30 percent of the women patients treated.

SUMM The combined use of the antiestrogen **Tamoxifen** and a luteinizing hormone-releasing hormone agonist, **Buserelin**, is also known for treatment of breast cancer. See, for instance, Klijn et al. J. Steroid Biochem. 420: no. 6B,. . .

SUMM . . . male animals including humans whose testicular hormonal secretions are blocked by surgical or chemical means, e.g., by use of an

LHRH agonist, e.g., [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10] **LHRH** ethylamide. The treatment includes administering an antiandrogen, e.g., flutamide in association with at least one inhibitor of sex steroid biosynthesis,. . .

SUMM U.S. Pat. No. 4,472,382 relates to a method of treating prostate cancer using the combination of an antiandrogen and an **LHRH** agonist.

SUMM . . . in the treatment of estrogen-related diseases. These diseases include, but are not limited to breast cancer, uterine cancer, ovarian cancer, **endometriosis**, uterine fibroma, precocious puberty and benign prostatic hyperplasia.

DETD When administered systemically, pharmaceuticals of the inventions may be used in the treatment of breast cancer, uterine cancer, ovarian cancer, **endometriosis**, uterine fibroma, precocious puberty and benign prostatic hyperplasia.

L10 ANSWER 17 OF 24 USPATFULL

AB Novel antiestrogenic compounds are disclosed for use in therapeutic preparations for treatment of estrogen-dependent diseases. The compounds are specified diphenylethane and diphenylethylene analogs which show strong affinity for estrogen receptors but substantially lack the capacity to activate such receptors or otherwise act as agonists.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	95:18454 USPATFULL	
TITLE:	Therapeutic antiestrogens	
INVENTOR(S):	Labrie, Fernand, Quebec, Canada Merand, Yves, Quebec, Canada	
PATENT ASSIGNEE(S):	Endorecherche, Inc., Quebec, Canada (non-U.S. corporation)	
	NUMBER	DATE
PATENT INFORMATION:	US 5393785	19950228 <--
APPLICATION INFO.:	US 92-913746	19920714 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 88-265150, filed on 31 Oct 1988, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Henley, III, Raymond J.	
ASSISTANT EXAMINER:	Criares, T. J.	
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)	
LINE COUNT:	564	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5393785 19950228 <--

SUMM H. Mouridsen et al., Cancer Treatm. Rev. 5 (1978) 131-141, discloses that **Tamoxifen**, an antiestrogen, is effective in remission of advanced breast cancer in about 30 percent of the women patients treated.

SUMM The combined use of the antiestrogen **Tamoxifen** and a luteinizing hormone-releasing hormone agonist, **Buserelin**, is also known for treatment of breast cancer. See, for instance, Klijn et al. J. Steroid Biochem. 420 (no. 6B). . .

SUMM . . . in the treatment of estrogen-related diseases. These diseases include, but are not limited to breast cancer, uterine cancer, ovarian cancer, **endometriosis**, uterine fibroma, precocious puberty and benign prostatic hyperplasia.

L10 ANSWER 18 OF 24 USPATFULL

AB Certain toxic compounds (T) such as, for example, compounds based upon diphtheria toxin, ricin toxin, pseudomonas exotoxin, .alpha.-amanitin, pokeweed antiviral protein (PAP), ribosome inhibiting proteins,

especially the ribosome inhibiting proteins of barley, wheat, corn, rye,
gelonin and abrin, as well as certain cytotoxic chemicals such as, for example, melphalan and daunomycin can be conjugated to certain analogs of gonadotropin-releasing hormone to form a class of compounds which, when injected into an animal, destroy the gonadotrophs of the animal's anterior pituitary gland. Hence such compounds may be used to sterilize such animals and/or to treat certain sex hormone related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	95:1591 USPATFULL
TITLE:	GnRH analogs for destroying gonadotrophs
INVENTOR(S):	Nett, Torrance M., Ft. Collins, CO, United States Glode, Leonard M., Aurora, CO, United States
PATENT ASSIGNEE(S):	Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5378688	19950103	<--
APPLICATION INFO.:	US 92-837639	19920214 (7)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 89-314653, filed on
23 Feb 1989, now abandoned

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Hill, Jr., Robert J.
ASSISTANT EXAMINER:	Davenport, A. M.
LEGAL REPRESENTATIVE:	Sheridan Ross & McIntosh
NUMBER OF CLAIMS:	3
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT:	1354

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5378688 19950103 <--

SUMM . . . of the steroidal hormones, estradiol, progesterone and testosterone. It should also be noted that the terms "GnRH" (gonadotropin-releasing hormone) and "**LHRH**" (luteinizing hormone-releasing hormone) are sometimes used interchangeably in the literature. For the purposes of describing the prior art both terms. . .

SUMM . . . regard was recently published in the INTERNATIONAL JOURNAL OF PHARMACOLOGY 76: R5-R8 by Singh et al. entitled "Controlled release of **LHRH**-DT from bioerodible hydrogel microspheres." Generally speaking, it teaches that a natural GnRH/diphtheria toxin can be used as
a vaccine. In this case the **LHRH**-DT molecule induces production of antibodies to GnRH which then serve to inactivate endogenous **LHRH** in the circulation. Without the endogenous **LHRH**, there is no stimulation of the anterior pituitary gland to secrete LH and the gonads will cease functioning. However, as. . .

SUMM . . . medicine as well. For example, the potential for achieving chemical castration (rather than "surgical" castration) with certain luteinizing hormone-releasing hormone (**LHRH**) analogs has been reported (see for example, Javadpour, N., Luteinizing Hormone-Releasing Hormone (**LHRH**) in Disseminated Prostatic Cancer; 1M, Vol. 9, No. 11, November 1988). Table I below gives the structure of **LHRH** and the structure of certain analogs (e.g., Goserelin, Leuprolide, **Buserelin** and Nafarelin) of **LHRH** which are capable of temporarily suppressing luteinizing hormone secretion and
thereby suppressing the gonads. As a consequence, these **LHRH** analogs have come to be regarded as a promising new class of agents for the treatment of various host-dependent diseases, especially prostatic cancer. In referring to Table I, it first should be noted that **LHRH** has a decapeptide structure and that substitution of certain amino acids in the sixth and tenth positions of the **LHRH**

produce analogs which render agonists that are up to 100 times more potent than the parent **LHRH** compound (hence these compounds are often referred to as "superagonists"). The structures of **LHRH** and the most commonly known **LHRH** superagonists are listed below.

SUMM

STRUCTURES OF **LHRH** AND SOME SUPERAGONISTS
(Superagonists have substitutions at positions 6 and 10)
##STR1##

SUPERAGONISTS:

Name	Subs. at 6	Subs. at 10	Terminator
Goserelin:	D-Ser(tBu)	AzaGly	Amide
Leuprolide:	D-Leu	des-Gly	Ethylamide
Buserelin:	D-Ser(tBu)	des-Gly	Ethylamide
Nafarelin:	D-2-NaphthylAla	None	Amide

SUMM . . . inhibit steroid-dependent tumor growth is through administration of counter-regulatory hormones (e.g., DES in prostate cancer), sex-steroid hormone binding inhibitors (e.g., **tamoxifen** in breast cancer) or surgical castration. Thus the potential medical uses of such chemical castration compounds are vast and varied.. . . appropriately administered sex steroids, desirable antifertility effects can be achieved. Another area of application in human medicine is treatment of **endometriosis**. This condition, which produces painful growth of endometrial tissue in the female peritoneum and pelvis also responds to inhibition of. . .

L10 ANSWER 19 OF 24 USPATFULL

AB Certain steroidal and non-steroidal compounds have been found to inhibit androgen and estrogen formation. Such inhibition may aid in the reduction of the activity of these hormones and may be useful in the treatment of diseases where, for example, inhibition of androgen or estrogen acitivity is desired. Preferred inhibitors also possess antiestrogenic activity, thus providing the advantage of a double inhibitory action both on estrogen formation and on estrogen action.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	94:99900 USPATFULL	
TITLE:	Inhibitors of sex steroid biosynthesis and methods for their production and use	
INVENTOR(S):	Labrie, Fernand, Quebec, Canada Merand, Yves, Quebec, Canada	
PATENT ASSIGNEE(S):	Endorecherche, Canada (non-U.S. corporation)	
	NUMBER	DATE
PATENT INFORMATION:	US 5364847	19941115 <--
APPLICATION INFO.:	US 92-966112	19921022 (7)
DISCLAIMER DATE:	20100420	
RELATED APPLN. INFO.:	Continuation of Ser. No. US 89-322154, filed on 10 Mar 1989, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Cintins, Marianne M.	
ASSISTANT EXAMINER:	Jordan, Kimberly R.	

LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1504
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5364847 19941115 <--
DETD . . . are not limited to, malignant as well as non-malignant steroid-sensitive diseases, especially brease cancer, prostate cancer, ovarian cancer, endometrial cancer, **endometriosis**, uterine leiomyomata, precocious puberty, hirsutism, acne, seborrhea, androgenic alopecia, benign prostatic hyperplasia, sexual deviants as well as for male and. . .
DETD In particular, a preferred inhibitor produces antisteroid effects at a dose possessing no agonistic activity, unlike compounds such as **Tamoxifen**, which possesses some agonistic properties which limit their therapeutical efficiency (Wakeling and Bowler, J. Steroid Biochem. 30, 141-147, 1988).
DETD . . . and antiandrogens are beneficial. In particular, this approach is of value in breast cancer, prostate cancer, endometrial cancer, ovarian cancer, **endometriosis**, benign prostatic hyperplasia, precocious puberty, hirsutism, acne, seborrhea, androgenic alopecia, menstrual disorders and as male and female contraceptive as well. . .
DETD . . . dosage of the above-described compound (multi sex hormone blocker) are the same as in intact patients or patients receiving an **LHRH** agonist or antagonist.

L10 ANSWER 20 OF 24 USPATFULL
AB A method of treatment or prevention of breast and endometrial cancer, osteoporosis and **endometriosis** in susceptible warm-blooded animals comprising administering a low dose of a progestin or other steroid derivative having androgenic activity and low masculinizing activity. Pharmaceutical compositions useful for such treatment and pharmaceutical kits containing such compositions are disclosed. An in vitro assay permitting specific measurements of androgenic activity of potentially useful compounds is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 94:97559 USPATFULL
TITLE: Methods of treating or preventing breast or endometrial cancer with low dose non-masculinizing androgenic compounds
INVENTOR(S): Labrie, Fernand, Quebec, Canada
PATENT ASSIGNEE(S): Endorecherche, Inc., Canada (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5362720	19941108	<--
APPLICATION INFO.:	US 93-15083	19930208 (8)	

RELATED APPLN. INFO.: Continuation of Ser. No. US 91-724532, filed on 28 Jun 1991, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Nutter, Nathan M.
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1452
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5362720 19941108 <--
AB A method of treatment or prevention of breast and endometrial cancer, osteoporosis and **endometriosis** in susceptible warm-blooded animals comprising administering a low dose of a progestin or other steroid derivative having androgenic activity and. . .

SUMM This invention relates to a method for treating or preventing breast and endometrial cancer, bone loss, and for treating **endometriosis** in susceptible warm-blooded animals including humans involving administration of a compound possessing androgenic activity, and to kits containing active ingredients. . .

SUMM . . . for breast and endometrial cancer as well as for the prevention and treatment of bone loss and for treatment of **endometriosis**. The main approaches for the treatment of already developed breast cancer are related to the inhibition of estrogen action and/or. . .

SUMM . . . two procedures giving irreversible castration. Recently, a reversible form of castration has been achieved by utilizing Luteinizing Hormone-Releasing Hormone Agonists (**LHRH** agonists) which, following inhibition of secretion of bioactive Luteinizing Hormone (LH) by the pituitary gland, decrease serum estrogens to castrated. . .

SUMM Several studies show that treatment of premenopausal breast cancer patients with **LHRH** agonists induces responses comparable to those achieved with other forms of castration (Klijn et al., J. Steroid Biochem. 20: 1381, 1984; Manni et al., Endocr. Rev. 7: 89=94, 1986). Beneficial effects of treatment with **LHRH** agonists have also been observed in postmenopausal women (Nicholson et al., J. Steroid Biochem. 23: 843-848, 1985).

SUMM U.S. Pat. No. 4,071,622 relates to the use of certain **LHRH** agonists against DMBA-induced mammary carcinoma in rats.

SUMM . . . No. 4,760,053 describes a treatment of selected sex steroid dependent cancers which includes various specified combinations of compounds selected from **LHRH** agonists, antiandrogens, antiestrogens and certain inhibitors of sex steroid biosynthesis.

SUMM . . . 4,472,382 relates to treatment of prostatic adenocarcinoma, benign prostatic hypertrophy and hormone-dependent mammary tumors with specified pharmaceuticals or combinations. Various **LHRH** agonists and antiandrogens are discussed.

SUMM . . . warm-blooded animals which may include inhibition of ovarian hormonal secretion by surgical means (ovariectomy) or chemical means (use of an **LHRH** agonist, e.g. [D-Trp.sup.6, des-Gly-NH.sub.2.sup.10]**LHRH** ethylamide, or antagonists) as part of a combination therapy. Antiestrogens, androgens, progestins, inhibitors of sex steroid formation (especially of 17.beta.-hydroxysteroid. . .

SUMM . . . months has recently been observed in a group of 33 postmenopausal women who previously failed or did not respond to **Tamoxifen** (Manni et al., Cancer 48: 2507-2509, 1981) upon treatment with Fluoxymesterone (Halostatin) (10 mg, b.i.d.). Of these women, 17 had. . . also undergone hypophysectomy. There was no difference in the response rate to Fluoxymesterone in patients who had previously responded to **Tamoxifen** and in those who had failed. Of the 17 patients who had failed to both **Tamoxifen** and hypophysectomy, 7 responded to Fluoxymesterone for an average duration of 10 months. Among these, two had not responded to either **Tamoxifen** or hypophysectomy.

SUMM The combination Fluoxymesterone and **Tamoxifen** has been shown to be superior to **Tamoxifen** alone. In fact, complete responses (CR) were seen only in the combination arm while 32% showed partial response (PR) in. . . Ann. Int. Med. 98: 139-144, 1983). Moreover, the median time from onset of therapy to treatment failure was longer with Fluoxymesterone+**Tamoxifen** (180 days) compared to the **Tamoxifen** arm alone (64 days). There was a tendency for improved survival in the combination therapy arm (380 versus 330 days).

SUMM . . . effect of an androgen combined with an antiestrogen is suggested by the report that patients who did not respond to **Tamoxifen** could respond to Fluoxymesterone and vice versa. Moreover, patients treated with **Tamoxifen** and crossing over to

Fluoxymesterone survived longer that those treated with the reverse regimen (Tormey et al., Ann. Int. Med.. . .

SUMM . . . unselected breast cancer patients (Horwitz, J. Steroid Biochem. 27: 447-457, 1987), an efficacy comparable to that of the nonsteroidal antiestrogen **tamoxifen** (Lippman, Semin. Oncol. 10 (Suppl.): 11-19, 1983). Its more general use, however, is for breast cancer relapsing after other endocrine. . .

SUMM High dose MPA as first treatment of breast cancer has shown similar effects as **Tamoxifen** (Van Veelen et al., Cancer 58: 7-13, 1986). High dose progestins, especially medroxyprogesterone acetate and megestrol acetate have also been. . . Am. J. Obstet. Gynecol. 158: 797-807, 1988). High dose MPA is being used with a success similar to that of **Tamoxifen** for the treatment of endometrial carcinoma (Rendina et al., Europ. J. Obstet. Gynecol. Reprod. Biol. 17: 285-291, 1984).

SUMM The androgen methyltestosterone has been shown to relieve the symptoms of **endometriosis** (Hamblen, South Med. J. 50: 743, 1987; Preston, Obstet, Gynecol. 2: 152, 1965). Androgenic and masculinizing side effects (sometimes irreversible). . .

SUMM . . . breast cancer, would have undesirable deleterious effects on bone mass in women. Similarly, blockade of estrogens, a common treatment for **endometriosis**, has similar undesirable deleterious effects on bone mass in women.

SUMM . . . object of the present invention to provide a method for prevention and treatment of breast cancer, endometrial cancer, osteoporosis and **endometriosis**, while substantially avoiding undesirable side effects.

SUMM . . . of said androgenic steroid described herein are particularly useful for the treatment of human breast or endometrial cancer, osteoporosis or **endometriosis**. It is believed that the methods are also suitable for all purposes which are enhanced by administering androgens or otherwise. . .

DETD . . . not only for their more rational use in the prevention and therapy of breast and endometrial cancers as well as **endometriois** and bone loss but also to avoid side effects caused by interaction with steroid receptors unnecessary for the desired beneficial. . .

DETD . . . breast and endometrial cancer as well as other diseases responsive to activation of the androgen receptor, e.g. bone loss and **endometriosis**. In this invention, the amount of the androgenic compounds administered is much lower than previously used in art for the. . .

DETD . . . scan, chest X-Ray, skeletal survey, ultrasonography of the liver and liver scan (if needed), CAT scan, MRI and physical examination. **Endometriosis** can be diagnosed following pains or symptoms associated with menstruations in women while definitive diagnosis can be obtained by laparascopy. . .

DETD . . . prevent other signs and symptoms of menopause. In women, when estrogen formation and/or action has been blocked for treatment of **endometriosis**, leiomyomata, breast cancer, uterine cancer, ovarian cancer or other estrogen-sensitive disease, administration of the androgen can be started at any. . .

DETD . . . for use in the prevention and treatment of breast and endometrial cancer as well as bone loss and treatment of **endometriosis** as discussed above. The kits or packages may also contain instructions on how to use the pharmaceutical compositions in accordance. . .

DETD . . . the above therapy using the described regimen, tumor growth of breast and endometrial cancer as well as bone loss and **endometriosis** can be relieved while minimizing adverse side effects. The use of the described regimen can also prevent appearance of the. . .

L10 ANSWER 21 OF 24 MEDLINE

AB In young women chronic use of luteinizing hormone releasing hormone (**LHRH**) agonists such as **buserelin** to treat **endometriosis** leads to estrogen-deficiency bone loss. **Tamoxifen** citrate is an estrogen agonist/antagonist which protects the skeleton from osteopenia when ovarian hormones are depleted. The present study was undertaken to determine whether **tamoxifen** citrate (20 mg/kg body wt/week s.c.) could prevent the osteopenic effect of **buserelin** (25 micrograms/kg body wt/day s.c.). Four groups of rats with 45Ca-labelled bones were studied for 4 weeks: group A--placebo controls; group B--**buserelin**; Group C--**tamoxifen**; group D--**buserelin+tamoxifen**. Bone resorption was monitored by measuring the urinary excretion of 45Ca and hydroxyproline. Interestingly **buserelin** lowered both blood 17 beta-estradiol values and uterine weights in the presence and absence of **tamoxifen**. However, **tamoxifen** slowed bone breakdown and inhibited the bone-thinning effects of **buserelin**. Total body calcium values (mg; means +/- S.D.) were: 2227 +/- 137; 1926 +/- 124; 2233 +/- 94 and 2268 +/- 163, in groups A to D respectively. Osteopenia was thus present only in group B (P less than 0.001). Because **tamoxifen** inhibits estrogen-deficiency bone loss in **buserelin**-treated rats without depressing the hypoestrogenic actions of this **LHRH**-agonist, we suggest that use of **tamoxifen** to protect the skeleton during **LHRH**-agonist therapy in young women should be explored. **Tamoxifen** citrate might also help to prevent postmenopausal osteoporosis.

ACCESSION NUMBER: 92404819 MEDLINE
DOCUMENT NUMBER: 92404819
TITLE: **Tamoxifen** in the rat prevents estrogen-deficiency bone loss elicited with the **LHRH** agonist **buserelin**.
AUTHOR: Goulding A; Gold E; Feng W
CORPORATE SOURCE: Department of Medicine, University of Otago Medical School, Dunedin, New Zealand..
SOURCE: BONE AND MINERAL, **(1992 Aug)** 18 (2) 143-52. Journal code: BMI. ISSN: 0169-6009.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212

TI **Tamoxifen** in the rat prevents estrogen-deficiency bone loss elicited with the **LHRH** agonist **buserelin**.
SO BONE AND MINERAL, **(1992 Aug)** 18 (2) 143-52. Journal code: BMI. ISSN: 0169-6009.
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CT . . .
chemically induced
Bone Diseases, Metabolic: PC, prevention & control
*Bone Resorption: CI, chemically induced
Bone Resorption: PC, prevention & control
***Buserelin: AI, antagonists & inhibitors**
Buserelin: PD, pharmacology
Calcium: ME, metabolism
Calcium: UR, urine
Disease Models, Animal
Drug Interactions
Estradiol: BL, blood
*Estrogens: DF, deficiency
Gonadorelin: ME, metabolism
Hydroxyproline: UR, urine
Organ Weight: DE, drug effects
Rats
Rats, Inbred Strains
***Tamoxifen: PD, pharmacology**
Uterus: DE, drug effects

RN **10540-29-1 (Tamoxifen)**; 33515-09-2 (Gonadorelin); 50-28-2 (Estradiol); 51-35-4 (Hydroxyproline); **57982-77-1 (Buserelin)**; 7440-70-2 (Calcium)

L10 ANSWER 22 OF 24 BIOSIS COPYRIGHT 1999 BIOSIS

AB **Tamoxifen** used for adjuvant therapy in breast cancer, has a complex and unclear action on endometrium and myometrium. Many authors demonstrated endometrial proliferous changes in peri and post menopausal women. Our study shows the development of **myomas** in three patients without uterine pathology before **tamoxifen** therapy, and the increase of a polyp and a **myoma** after **tamoxifen** therapy. Moreover, we observed the development of a **myoma** in a patient after one year **tamoxifen** in association with **LHRH** analogue therapy. It is necessary to continue our study with a larger number of patients to assess the hyperplasia effect of **tamoxifen**.

ACCESSION NUMBER: 1993:345129 BIOSIS
DOCUMENT NUMBER: PREV199396042129
TITLE: Uterine changes during **tamoxifen** therapy.
AUTHOR(S): Rullo, S.; Tagliaferri, T.; Bandiera, F.; Fiorelli, C.; Felici, A.; Piccioni, M. G.; Framarino Dei Malatesta, M. L.
(1)
CORPORATE SOURCE: (1) III Clin. Osterica Ginecol., Univ. di Roma "La Sapienza", Policlin. Umberto I, 00161 Roma Italy
SOURCE: Clinical and Experimental Obstetrics & Gynecology, (1993) Vol. 20, No. 2, pp. 116-119.
ISSN: 0390-6663.
DOCUMENT TYPE: Article
LANGUAGE: English

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ISSN: 0390-6663.
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IT Major Concepts
Development; Oncology (Human Medicine, Medical Sciences); Pharmacology; Reproductive System (Reproduction); Toxicology

IT Chemicals & Biochemicals
TAMOXIFEN

RN 10540-29-1 (**TAMOXIFEN**)

L10 ANSWER 23 OF 24 BIOSIS COPYRIGHT 1999 BIOSIS

AB The effect of medical oophorectomy induced by treatment with the luteinizing hormone-releasing hormone (LH-RH) agonist[D-Trp6,des-Gly-NH210]LH-RH ethylamide was studied in 34 patients with laparoscopically proven **endometriosis**. **Tamoxifen** was administered during the 1st month of therapy to prevent flare-up of the disease during the estrogen surge. Fifteen women had a decrease of their laparoscopy scores translated into an improvement in the stage of disease, whereas in 12 others, the decrease in their scores was not enough to allow a change of disease stage. The 2nd laparoscopy was not performed in 7 women. Medical oophorectomy, after daily injection of the LH-RH agonist (LH-RH-a), was accompanied by low levels of circulating estradiol. The serum concentration of all .DELTA.4-3-ketosteroids was significantly decreased during medical oophorectomy, whereas the level of circulating .DELTA.5-3.beta.-hydroxysteroids was not altered except for pregnenolone. The present data indicate that medical oophorectomy induced by an LH-RH-a in association with **tamoxifen** is a very efficient and well tolerated therapy in **endometriosis**.

ACCESSION NUMBER: 1990:452916 BIOSIS
DOCUMENT NUMBER: BA90:103556
TITLE: HORMONAL AND BIOCHEMICAL CHANGES DURING TREATMENT OF **ENDOMETRIOSIS** WITH THE LUTEINIZING HORMONE-RELEASING HORMONE **LHRH** AGONIST D TRP-6 DES-GLY-AMIDE-10 **LHRH** ETHYLAMIDE.
AUTHOR(S): DUPONT A; DUPONT P; BELANGER A; MAILOUX J; CUSAN L; LABRIE F
CORPORATE SOURCE: LAB. MOL. ENDOCRINOL., CHUL RES. CENT., 2705 LAURIER BLVD., QUEBEC G1V 4G2, QUEBEC, CANADA.
SOURCE: FERTIL STERIL, (1990) 54 (2), 227-232.
CODEN: FESTAS. ISSN: 0015-0282.
FILE SEGMENT: BA; OLD
LANGUAGE: English

TI HORMONAL AND BIOCHEMICAL CHANGES DURING TREATMENT OF **ENDOMETRIOSIS** WITH THE LUTEINIZING HORMONE-RELEASING HORMONE **LHRH** AGONIST D TRP-6 DES-GLY-AMIDE-10 **LHRH** ETHYLAMIDE.

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IT Miscellaneous Descriptors
HUMAN DECAPEPTYL **TAMOXIFEN** METABOLIC-DRUG ESTRADIOL INFERTILITY OOPHORECTOMY

RN 50-28-2 (ESTRADIOL)

9002-67-9 (LUTEINIZING HORMONE)
9034-40-6 (**LHRH**)
10540-29-1 (**TAMOXIFEN**)
57773-63-4 (DECAPEPTYL)

L10 ANSWER 24 OF 24 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1986:288328 BIOSIS
DOCUMENT NUMBER: BR31:22906
TITLE: CONTROL OF UTERINE **MYOMA** AND CORPUS CARCINOMA USING HORMONES.
AUTHOR(S): KATO H
SOURCE: Rinsho Fujinka Sanka, (1986) 40 (1), 63-65.
CODEN: RFUSA4. ISSN: 0386-9865.
FILE SEGMENT: BR; OLD
LANGUAGE: Japanese
TI CONTROL OF UTERINE **MYOMA** AND CORPUS CARCINOMA USING HORMONES.
SO Rinsho Fujinka Sanka, (1986) 40 (1), 63-65.
CODEN: RFUSA4. ISSN: 0386-9865.
IT Miscellaneous Descriptors
HUMAN MEGESTROL ACETATE **TAMOXIFEN** CITRATE R-2323 GESTRINONE HYDROPROGESTERONE CAPROATE MEDROXYPROGESTERONE ACETATE ANTINEOPLASTIC-DRUG HORMONE-DRUG **LHRH** TARGET ORGAN
RN 71-58-9 (MEDROXYPROGESTERONE ACETATE)
595-33-5 (MEGESTROL ACETATE)
9034-40-6 (**LHRH**)
16320-04-0 (R-2323)
16320-04-0 (GESTRINONE)
54965-24-1 (**TAMOXIFEN** CITRATE)